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A PRELIMINARY STUDY OF THE EXPERIMENTAL ASPECTS OF IODID AND BROMID EXANTHEMS *

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The experimental aspects of the various dermatoses associated with and following the ingestion of various medicaments have received little attention from dermatologists. This is quite readily understandable when one realizes that such investigation involves the most intricate problems of biochemical and physicochemical research. For this reason, therefore, most of the articles dealing with the question of drug eruptions from their experimental side have been written by physiologic chemists.

Notwithstanding the fact that most of our experimental evidence comes from those not primarily interested in dermatology, valuable contributions from the side of cutaneous medicine have been made, in calling attention to the appearance of such rashes and in properly ascribing the cause to the offending drug. We are, therefore, indebted to dermatologic literature for the first descriptions and the etiologic factors involved; and, moreover, in not a few cases, to productive research attempting to explain the ultimate cause.

With the introduction into the practice of medicine, notably in the last three decades, of an enormous number of synthetic drugs, there has been a correspondingly increasing number of cases of so-called idiosyncrasy or susceptibility to such medicaments, such being mani-

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fested by reactions on the part of the digestive, the nervous and the arterial systems, and, most important, the cutaneous covering. It is safe to state that probably no synthetic drug has ever yet been introduced which, in isolated cases, has not given rise to symptoms of intolerance, with their associated cutaneous manifestations. These, as is well known, vary from the most evanescent type of erythema to lesions actually so destructive as to impair function and to endanger life. The greatest diversity of lesion and the greatest variability of intensity can occur with each and any drug; the process is the same, the difference only in the intensity of the reaction.

Lacking accurate experimental evidence, the occurrence of exanthems following the ingestion of drugs has been ascribed by various writers to such vague terms as idiosyncrasy, susceptibility, chemotaxis, toxicity, and, of late years, allergy and anaphylaxis.

Granting that, in enormous doses, practically all drugs of therapeutic value are distinctly toxic to the human organism, it is evident from the outset that, in a given case of intolerant reaction to such drug on the part of the skin, two factors surely come into consideration: (1) the poisonous quality of the drug itself, and (2) the human organism in its relation to the drug. All synthetics, and most drugs, are prepared with extreme care with regard to their actual toxicity, long before their introduction into medical practice. Their therapeutic application, moreover, is always fixed at a point much below the minimum lethal dose. The natural source for investigation as to the effect of the minimum lethal dose on the person who nevertheless reacts is in the person himself.

Some drugs in common use are so frequently associated with mild manifestations on the skin that the occurrence of these manifestations is regarded as almost physiologic. Thus, for example, as is well known, pustulation occurs so frequently in the administration of iodid of potash that it is stated by some that iodid only reaches its physiologic effect when the skin reacts in the form of pustules. We believe this conception to be quite as erroneous as the former acceptance of the physiologic reaction of mercury when the stage of salivation had been reached.

Exanthems following the ingestion of synthetics, although common enough, occur usually in isolated instances, and the manifestations are, as a rule, of such a fleeting nature that the investigation of these eruptions from the biochemical side is extremely difficult, owing to the lack, over a sufficient period of time, of the proper material. Laboratory animals, furthermore, do not lend themselves readily to experimentation for this purpose.

The universal use, notably in group cases, of iodids in the infectious granulomas, and of bromids in neurologic disorders, such as epilepsy,

has for obvious reasons, therefore, led to a greater degree of experimentation with these two drugs than with any others. It is highly probable, also, that a suitable explanation, based on proper experimentation, for the occurrence of iododermas and bromodermas in their various forms would suffice as an adequate explanation for the occurrence of exanthems and rashes due to the ingestion of other drugs. The bromids have been more extensively investigated than have the iodids.

Notable contributions in foreign literature bearing on the subject have been made by Adamkiewicz,[1] Szadek,[2] Laudenheimer,[3] Von Wyss,[4] Ulrich,[5] Ellinger and Kotake;[6] and in this country by Sollman and Pilcher,[7] Kolmer and his associates,[8] Engman and Mook,[9] and by Osborne.[10] The earliest investigators on the subjects of both bromid and iodid were led to believe that the reaction in the skin was due to the liberation of the free halogen in the blood, and its irritant action directly on the skin or on the blood vessels of the skin. Color, perhaps, was lent to this view by the discovery that all of the secretions of the body contained the offending drug, after ingestion. All glandular

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1. Adamkiewicz: Die Ausscheidungswege des Jodkaliums beim Menschen, Charité-Ann. **3**:381, 1878.

2. Szadek: Casuistik des Brom-exanthems, Arch. f. Derm. **20**:599, 1888.

3. Laudenheimer: Ueber das Verhalten der Bromsälze im Korper in des Epileptikers, Neurol. Centralbl. **16**:538, 1897.

4. Von Wyss: Ueber das Verhalten der Bromsaltzer in menschlichem und tiereschen Organismus, Arch. f. exper. Path. u. Pharmakol. **55**:263, 1906: Ueber das Verhalten der Bromsaltzer in menschlichem und tiereschen Organismus, Arch. f. exper. Path. u. Pharmakol. **59**:186, 1908. Von Wyss and Ulrich: Die Bromtherapie der Epilepsie auf experimenteller Grundlage, Arch. f. Psychiat. **46**:197, 1909-1910.

5. Ulrich: Footnote 4, third reference.

6. Ellinger and Kotake: Die Verteilung des Broms im Organismus nach darreichung unorganischer und organischer Brompreparata, Arch. f. exper. Path. u. Pharmakol. **65**:87, 1911.

7. Sollmann and Pilcher: Endermic Reactions, J. Pharmacol. & Exper. Therap. **9**:309, 1916-1917; ibid. **10**:147, 1917. Sollmann: The Fate of Iodin, Iodids and Iodates in the Body, J. Pharmacol. & Exper. Therap. **9**:279, 1917.

8. Kolmer, J. A.; Matsunami, Toitsu, and Broadwell, Stuart, Jr.: The Effect of Potassium Iodid in the Luetin Reaction, J. A. M. A. **67**:718 (Sept. 2) 1916. Kolmer, Immerman, Matsunami and Montgomery: The Effect of Certain Drugs upon Skin Reactions, J. Lab. & Clin. Med. **2**:401, 1916-1917. Kolmer: Mechanism and Clinical Significance of Anaphylactic and Pseudo-Anaphylactic Skin Reactions, Proc. Pan-Am. Scien. Cong., Sec. 8, Pub. Health & Med. **10**: 287, 1917.

9. Engman and Mook: A Contribution to the Histopathology and History of Drug Exanthems, J. Cutan. Dis. **24**:502, 1906.

10. Osborne, E. D.: Iodid in the Cerebrospinal Fluid, with Special Reference to Iodid Therapy, J. A. M. A. **76**:1384 (May 21) 1921.

structures, including the sebaceous glands and sweat coils, eliminated the drug, and, in the case of the latter, the elimination took place on the surface of the body. The acid reaction in secretions from the sweat and sebaceous glands was thought by earlier observers to liberate iodid and bromid in their free state, with the resultant irritation phenomena.

As early as 1878, Guttman [11] reported the occurrence of bromid in the contents of pustules in a patient taking 12 gm. of bromid a day. This observation, however, has not been confirmed by subsequent investigations. In the same year, Adamkiewicz,[1] investigating iodid, established its presence in all body fluids following ingestion, and stated that he had found it also in the pus of iodid acne, using as his reagent a starch paste for its detection. Both of these observers regarded the cutaneous reaction as due to the free halogen liberated by the acid with which it came in contact in and about the structures of the skin.

It is noteworthy that, in 1885, Tilbury Fox,[12] in reporting a case of bromoderma, stated that the histologic examination of the lesions did not bear out this theory, in that, in his case, neither sebaceous nor sudoriparous glands were found to be in the least involved in the process. In 1888, Szadek,[2] after studying bromodermas and establishing that these varied from simple erythema to urticaria, nodules, bullae and phlyctenulae, came to conclusions similar to those held by Guttman.[11] From his chemical studies and the histologic study of Neumann, he regarded the bromexanthem as starting in an irritation phenomenon from the sebaceous apparatus.

This belief, namely, that the native halogen was, by an actual irritation, responsible for the eruption, persisted until about 1897, and, in the face of experimental evidence to the contrary, is still held by some. At this time, Laudenheimer,[3] with much material for the study of epilepsy at his disposal, made a careful chemical observation of the behavior of bromid in the various tissues of the body in a large number of patients. He demonstrated a very definite phenomenon for bromid, which differs materially from the behavior of either chlorid or iodid in the body. His researches, subsequently substantiated in 1910 by Von Wyss,[13] and since that time by others, demonstrated that the ingestion of bromid led to a gradual piling up of the drug and a gradual replacement by it of the chlorid content of the tissues. That is to say, a patient taking bromid at once showed in the urine a marked increase

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11. Guttman: Bromreaktion des Inhalts von Aknepustuln nachlangen Bromkaliumgebrauch in einem Falle von Agrophobie, Virchows Arch. f. path. Anat. **74**:541, 1878.

12. Fox, Tilbury: Brom Eruption, Brit. M. J. **2**:971, 1885.

13. Von Wyss: Footnote 4, third reference.

of a chlorid excretion. The bromid at the outset was excreted by the urine in far smaller quantities than it was ingested. Not only did this take place in the circulating blood, but it was demonstrated that the chlorin ion of the gastric juice was replaced by bromin (Nencki and Simanowski [14]). The various symptoms of brominism, apart from the cutaneous reactions, namely, stupor, pallor, emaciation and psychic disturbance, Laudenheimer attempted to explain as manifestations of chlorid hunger or chlorid deficiency. This is interesting in substantiation of his explanation that the reintroduction of large amounts of chlorid into the system gradually reestablished the normal chlorid content of the tissues, with a relief of the symptoms of bromism. It is also interesting, in this connection, that the introduction of chlorid in excess into the system has a marked beneficial effect upon the bromodermas.

Similar investigations conducted by Nencki and Simanowski,[14] Von Wyss,[4] and also Ulrich,[5] and by Büchner and Fessell,[15] substantiated the results of Laudenheimer. Fessell [15] showed that chlorid elimination markedly increased, as evidenced by its appearance in the urine after bromid intake, and that, further, after bromid and sodium chlorid were given together, the bromid was much more rapidly eliminated. Von Wyss,[16] and later Von Wyss and Ulrich,[17] in a careful study of the behavior of bromid in the animal and human organism, showed definitely that the elimination lagged far behind the intake, and that long after the withdrawal of the drug its presence could be detected in the urine. Von Wyss stated that if this were so, either bromin remained somewhere in the body in close union and bound up with protoplasm, or else it remained not fixed but, for some unknown reason, not as readily eliminated by the kidney, as iodid and chlorid; or that it is eliminated into the intestine and continually reabsorbed, being slowly eliminated by the kidney, establishing thus a more or less continuous digestive cycle for the drug. By intracutaneous injection, he determined that the chlorin ion could be displaced in the gastric juice of the stomach by the bromin ion. He concluded that bromid in the body is removed slowly, for some unknown reason, through the kidney, and that a constant reabsorption by the gastric and intestinal mucosae occurs; which accounted for its piling up in the system. He further determined, by careful tissue analysis, that the circulating blood, and notably the serum, contained the bulk of the bromid held back in the

14. Nencki and Simanowski: Studien über das Chlor und die Halogene im Thierkörper, Arch. f. exper. Path. u. Pharmakol. **34**:313, 1894.

15. Fessell: Ueber das Verhalten des Brom im Thierkörper, München. med. Wchnschr., Series 2 **46**:270, 1899.

16. Von Wyss: Footnote 4, first reference.

17. Von Wyss and Ulrich: Footnote 4, third reference.

system. The remarkable ability of bromid to replace chlorid was further established by the interesting findings of Ellinger and Kotake,[6] who, by careful chemical quantitative analysis, determined that those organs and tissues in which there were the largest amounts of chlorid contained the largest amount of bromid, in experimental animals to whom bromin had been fed.

Von Wyss and Ulrich [17] did not regard the cutaneous manifestations of bromid ingestion as symptomatic of bromid intoxication, nor in any way related to what they were pleased to call chlorid deficiency in the explanation of other forms of brominism. They regarded the cutaneous lesions as due to the liberation of free bromin on the skin, giving rise to exquisite irritation phenomena, thereby enabling the existing pus organisms on the skin to become pathogenic, with the resultant formation of the lesion. Laudenheimer,[3] however, was inclined to regard the cutaneous reaction as actually a symptom of brominism, that is, as due to chlorid deficiency.

In 1906, a noteworthy article appeared in the French literature by Pasini.[18] His contribution is valuable because he demonstrated that it was quite impossible for free bromin to exist in the pus, as was recorded by Guttman;[11] that if one added actual bromid in vitro to albumin solutions, it was impossible to detect the drug until the albumin was destroyed, or until such a high degree of oxidation occurred by the addition of concentracted acid that it could be liberated; and that this degree of acidity could never occur in the normal chemistry of the animal body. Following experiments involving the implantation of actual bromids subcutaneously into laboratory animals, he stated his belief that the salts of bromin exercised a chematactic action, and that resultant cutaneous reaction was one of chemical irritation.

These views were held tenable by Jacquet, Leloir and Vidal [19] only so far as such irritation prepared the soil for subsequent activity of the common pus organisms. About the same time, Auspitz, and also Crocker,[20] advanced the theory that the cutaneous reactions were due to a direct action of the drug on the vasomoter centers.

In 1906, Engman and Mook [9] presented a paper before the American Dermatological Association on the "Histopathology and the Theory of Drug Eruptions." Their contribution is noteworthy in that they stated that the pustular contents of iodid and bromid eruptions, not only in simple pustules but also in open ulcers, were sterile, and that the micro-organisms of the skin could, therefore, not be held

18. Pasini: Sur la pathogenie des eruption bromiques, Ann. de dermat. et syph., Series 4 **7**:1, 1906.

19. Jacquet, Leloir and Vidal: Etude d'un cas de bromisme cutané polymorphe, Ann. de dermat. et syph., 1889, p. 981.

20. Crocker: Eruptions from Bromid and Iodid, Brit. M. J. **2**:1208, 1893.

responsible for the appearance of the lesions. They likewise called attention to the tendency of iodid and bromid eruptions to localize themselves in the seborrhic and acne areas. Another interesting point in connection with their presentation was the demonstration of iodid in the pus from iodid lesions. Bromid was not satisfactorily investigated in their cases, on account of the difficulty of finding a specific bromid reaction. In their contribution, Engman and Mook express the opinion that the lesions resulting from the ingestion of both drugs are liable to occur at points of previous inflammation, that actual trauma may precipitate an eruption, and that the glands or follicles of the skin take no specific part in the production of the lesions. They suggest a disturbance of equilibrium induced by various factors producing a toxin, which in turn causes irritation and various local inflammatory symptoms. Herein is the first suggestion that, in the occurrence of bromid and iodid lesions, an altered disturbance of the blood might be held responsible.

Considerable impetus to the study of the mechanism of all drug exanthems, notably those caused by iodid and bromid, was given by the careful studies of Kolmer and his associates,[8] and of Sollmann.[21] Sollmann's and Pilcher's [7] studies were carried out with the idea of determining the local effect of various drugs on the production of cutaneous lesions. An enormous number of drugs were tried out, both by intracutaneous inoculation and by the ingenious use of the *Mucuna* method. This consists in the application of the dried stiff hairs of a leguminous seedpod, rubbing these on the skin, and following it by solutions of the drugs to be investigated. In a later study, Sollmann [21] investigated the fate of iodin, iodids and iodates in the body. His studies led him to the inevitable conclusion that iodin exists in the tissues of the body only as iodid, that it could never be liberated free in the body or from the body surface, because to liberate the free halogen would require a hydrogen-ion content, that is to say, an acidity far stronger than can possibly exist in the human organism. He also demonstrated that the iodin existed loosely bound with protein, in which it was readily dialyzable.

Kolmer [22] investigated the behavior of iodid and drug exanthems from the side of a possible allergy or anaphylaxis. In an extensive monograph published in 1917, Kolmer [23] concludes that skin reactions are either specific anaphylactic in nature; pseudospecific or nonspecific protein reactions; or traumatic reactions; that iodid and bromid increase the nonspecific action by facilitating the activity of nonspecific pro-

21. Sollmann, Torald: Footnote 7, third reference.
22. Kolmer: Footnote 8, first and second references.
23. Kolmer: Footnote 8, second reference.

teolytic ferments and the production of protein poison through the removal of antiferment. It will be noted here that this bears directly on the administration of iodid and bromid as they affect anaphylactic conditions caused by protein poison, and is in no way an attempt to explain the mechanism of iododermas and bromodermas. The suggestion, however, that the presence of iodid and bromid in the blood can and does materially affect true allergic reactions no doubt bears in a very distinct way on the nature of reactions caused by these drugs themselves. Kolmer's investigations in this field were inspired by the work of Sherrick,[24] who, in 1915, determined that nonsyphilitic patients could be made to react with a typical pustule with the luetin test, if before or after the test was made they were taking iodid of potash.

In summing up the total evidence at present in our hands, we are confronted with a mass of contradictory facts:

1. The theory that iododermas and bromodermas can be caused by the liberation and the presence of the free halogen in the tissues.

2. That the presence of the salts of these halogens increases the virulence of the normal cocci of the skin, with resulting infection.

3. That they are the phenomena of chemical irritation.

4. That they are vasomotor phenomena.

5. That they are due to an altered condition of the blood, and that the lesions themselves are sterile.

6. That they are closely allied to the phenomena of local sensitization or allergy.

It was in an attempt to shed at least some light on this problem that the studies herein noted were begun about a year and a half ago.

Our experiments covered the following problems:

1. The corroboration of previous results for the determination of iodid and bromid in body fluids.

2. The study of the elimination of bromid in the urine and the replacement of chlorid by it in the tissues.

3. Investigation as to the presence of iodin and bromin or their salts in the local lesions of bromoderma and ioderma.

4. Bacteriologic studies of the lesions to determine the absence or presence of pus organisms.

5. Percutaneous tests on patients taking salts of bromin and iodin, in the attempt to determine a skin sensitization.

6. An attempt to produce cutaneous bromid reaction in conditions of acidosis.

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24. Sherrick, J. W.: The Effect of Potassium Iodid in the Luetin Reaction, J. A. M. A. **65**:404 (July 31) 1915.

7. The investigation as to the existence of specific precipitins in the blood for bromid and iodid.

With respect to the determination of bromid and iodid in the body fluids, it may be briefly stated that in the case of iodid this is a matter of extreme ease. In tissues containing organic material, such as the circulating blood, it is, however, necessary, before testing for either iodid and bromid, to destroy the organic material. We found the easiest way to do this was by digesting the organic material with sulphuric acid, distilling the material, and testing for the drug in the acidulated distillate. The final test employed was that of shaking out iodin with either chloroform or carbon disulphid in the presence of nitric acid and sodium nitrite. Under these conditions, iodin was found, even if only a small quantity had been ingested, in the circulating blood, the urine, the sweat and the saliva. So delicate was our test under these conditions that we could determine easily the presence of iodin in 10 c.c. of blood fifteen minutes after the ingestion of 5 grains (0.3 gm.) of potassium iodid. After distilling over and acidulating the distillate, even a few drops of the original 10 c.c. were found to contain iodin.

In the case of bromid, great difficulty was encountered in that the established chemical tests for bromid are markedly interfered with by the presence of chlorid. We finally determined on the best method for the detection of bromid as follows: The suspected material was oxidized with a solution of potassium permanganate in the excess of sulphuric acid. In organic material, this maneuver was carried out as in the case of testing for iodid by first digesting with sulphuric acid and distilling. Under these condition, we found bromin in patients ingesting the drug, in the blood, the urine, the sweat and the saliva, under the same circumstances that iodin was found.

In our investigations, we had an opportunity of making tests in a large number of cases, the patients in the iodid group being syphilitic and having taken the drug over a long period of time, and the patients in the bromid group, for the most part, being afflicted with and treated for various neurologic disturbances, including epilepsy. In no case were we able to determine the presence of the slightest trace of either drug in the local lesions, and it is our belief that this does not occur, except so far as there may be an admixture of the blood serum in the local lesion. We examined at one time an enormous amount of pus gathered from several patients, who were taking large amounts of iodid. The addition of the smallest quantity of iodid of soda (2 or 3 drops to a 1 : 1000 solution) to such a mixture, followed by dilution, enabled us to determine iodid very readily. In the sample, however, in which iodid existed as a possible unknown, that is to say, in the pure pus recovered from many pustules from several different patients, our

most delicate test failed to reveal a trace of the drug. It should be noted here that our test is much more delicate than the test with starch paste.

In this connection, attention might well be called to the enormous nodular bromoderma which not so infrequently occurs in nursing infants whose mothers are taking bromid for epilepsy, or other cause. The largest amount of such bromid ingested by the mother is voided in the urine, and but a small amount exists in the milk. It is hardly conceivable, therefore, that in such cases an enormous lesion could be caused by the actual presence of the drug itself.

In the blister content in all cases in which iodid and bromid are ingested, both drugs were easily recoverable.

The belief that the typical iodid acne is a physiologic reaction we believe to be erroneous. We found that a large number of patients could take relatively enormous doses of iodid without the slightest sign of a pustule, and we were able to establish, moreover, that when a tendency to pustulation occurred, it apparently bore no relation to the amount of the drug given. Patients receiving such small amounts as 5 or 10 grains (0.3 to 0.6 gm.) developed a rash at times; others again, under like conditions, maintained over many weeks, developed no pustules. The same condition pertained to doses as high as 200 grains (13 gm.) per diem; some reacted with pustulation; others, under like conditions, did not.

We can corroborate the findings of Engman and Mook that patients who had a pre-existing acne or seborrhea seemed to develop the acne more readily than did others.

It is regrettable that we had no opportunity to examine the contents of a bullous iododerma. If the contents of such bullae are analogous to the fluid of an artificial blister, one might expect in such cases to find the salt present.

To determine the excretion of chlorids in patients taking bromid, twenty-four hour urine was examined from day to day with respect to the chlorid content. It is to be noted that the normal chlorid content of the urine varies so greatly that a normal had to be fixed for each case before the necessary examinations could be made. Having established the normal for the individual, it was noted, after the ingestion of bromid, that an increase in chlorid output began about the second or third day, this increasing markedly up to about twice the amount of normal for that individual; after which a gradual fall toward normal occurred, notwithstanding the fact that the drug was continued during this time. The normal, however, was not reached in these cases until a considerable time after the drug had been withdrawn.

A most interesting observation in this connection occurred in a case of pemphigus. The patient received potassium bromid, 20 grains

(1.3 gm.) three times daily. About the third day after this had been begun, he broke out with an enormous crop of new blisters. The contents of these blisters were found to contain bromin, more easily demonstrable than in any other material examined. The urine showed a slight increase in chlorid at the outset, and a decided fall after the appearance of the blisters. After this fall, the amount remained well below the patient's normal.

In the investigation of the behavior of iodid toward the normal chlorid in the urine, no change was found. This is entirely in accordance with the fact that iodid is readily and rapidly eliminated through the kidneys. A suggestion is here tenable that the ultimate mechanism of iododerma may differ materially from that of bromoderma.

In our bacteriologic studies, in cases of iododerma and bromoderma, we were unable to substantiate the result of Engman and Mook in finding such lesions sterile. Cultures from pustules were made with great care, the lesions being first cauterized and the cultures being made from the depth of the lesions. All cases examined revealed uniformly large colonies of staphylococci.

To determine whether or not there existed in normal patients not ingesting either drug, and in those partaking of the drug, a cutaneous sensitization, solutions of potassium bromid and potassium iodid were injected cutaneously and intracutaneously. For the normals, we ourselves were the controls. The remainder of the skin tests were carried out on patients ingesting either salt. From our studies thus conducted, it was found that no cutaneous sensitization could be determined, either in patients already ingesting iodid and bromid, or in those not ingesting it who subsequently might develop pustulation. All cases, both of controls and of individuals ingesting the drug, were negative to percutaneous tests, both injections and scarifications.

When a certain concentration of both salts had been reached (the saturated solution), minute abscesses, in no way to be regarded as specific reactions, occurred in all cases.

Investigation of the effect of bromids in patients suffering with acidosis was based on the possible assumption that the replacement of chlorid in the blood by bromid might lead to a change in the blood reaction. It is a well-known fact that patients in a state of cachexia and acidosis are extremely prone to auto-infection, with the development of furuncles and carbuncles. Such conditions are frequently seen in the acidosis of diabetes and starvation, and the acidosis of marasmus, in malnutrition, and in the cachexia following acute infectious fevers. The suggestion followed here was that the local lesions following ingestion of the bromid might possibly be infections in the skin due to an altered alkaline reaction in the blood. To determine this, bromid in small doses was given to diabetic persons and to patients

who, for other reasons, were suffering from milder or severer grades of acidosis, it having been recognized that the administration of small amounts of the drug could in no way be harmful to these patients. In no case did the administration of bromid under these conditions result in a spontaneous bromoderma.

To determine under such conditions whether a protein injected into the skin could in this way influence the production of a lesion, tiny droplets of typhoid vaccine were injected intracutaneously at various sites. These injections were followed in a few days, in a patient receiving a small amount of bromid, by the appearance of pustules entirely analogous to those of the pustular bromoderma. They persisted but a short time, however, and disappeared even during the time that the patient was ingesting bromid.

In order to determine the possible existence of precipitins in the blood which might perhaps be held responsible, or in some way allied to the local phenomena, small amounts of varying solutions of iodid of potash and bromid of potash were added to the blood serums of patients ingesting both drugs, as well as to normal bloods. It is conceivable that our technic was at fault, but we must, for the present, report uniformly negative results in these experiments.

COMMENT

From our results, certain definite things appear to have been established:

1. The pustules of iodid, also of bromid, acne are not sterile. Bacteria, therefore, cannot be eliminated as a factor, possibly, and probably, secondary in the production of such lesions. That they cannot be primary is undoubtedly shown by the fact that certain forms, at least of the cutaneous manifestations following the ingestion of these drugs, do not occur as pustules. The erythematous, urticarial and pure bullous types cannot in any way be associated with a bacterial cause.

2. Iodid and bromid exist in the body fluids following their ingestion, but are not found in the purulent material from acneform lesions. Their easy demonstration in the sweat, and their presence in the highest concentration in the blood serum, no doubt accounts for their previously reported presence in the local lesions as a contamination.

3. Percutaneous sensitization tests for iodid and bromid are uniformly negative, and cannot, therefore, be used to indicate ingestion susceptibility.

4. The ready substitution in the body fluids of chlorid by bromid leads to the hypothesis that the ultimate cause of this reaction in the skin differs somewhat from that caused by iodid. This replacement

may well lead to a change in the reaction of the circulating blood, and such change, it is conceived, might readly play a part in the production of bromid lesions.

5. The percutaneous introduction of foreign protein in the presence of a circulating blood containing bromid resulted, in one case, in lesions simulating those caused by bromids spontaneously. This reaction is, no doubt, parallel to the experiment of Sherrick with luetin in the presence of circulating iodid.

6. Precipitins in the blood serum were not demonstrable, at least by the addition in vitro of solutions, in minute quantities, of bromid and iodid salts to the blood serums.

7. The local phenomena of iododerma and bromoderma do not find their explanation on simple bacterial nor simple chemical grounds. The ultimate explanation probably lies in a complex biochemical reaction. The classification of such cutaneous phenomena, however, as true sensitization or allergy is as yet unjustifiable in the light of present knowledge.

DRUG ERUPTIONS FROM THE CLINICAL ASPECT

WITH SPECIAL REFERENCE TO THE RECENT MEDICAMENTS *

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Whoever has read Prince A. Morrow's [1] monograph on drug eruptions will surely sympathize with us in our effort to present the subject of "Drug Eruptions from the Clinical Aspect" with the greatest possible expedition; with Morrow's work before us, we feel that little more can be said. The eruptions of his day are, with a few additional examples, those of today. The best course to follow, it seems to us, is to forbear from burdening you with a reiteration of the well-known cutaneous manifestations resulting from the use and abuse of the older drugs, and to devote what time and space is at our disposal to a consideration of eruptions provoked by the recent medicaments. Among the latter are included such widely used drugs as barbital, medinal, adalin, bromural, phenobarbital (luminal), cinchophen, pyramidon, melubrin, acetylsalicylic acid, hexamethylenamin, phenolphthalein and the various arsphenamins.

DEFINITION

As used today, the term "drug eruptions" is synonymous with dermatitis medicamentosa; that is, eruptions resulting from the introduction into the body of drugs which undergo absorption and elimination. The older definition of the term "drug eruption" embraces a much broader field and is interpreted by Morrow in this sentence: "In the proper signification of the term, drug eruptions embrace all congestive and inflammatory changes in the skin caused by the external and internal use of drugs."[2] Today, the term dermatitis venenata is used to designate eruptions resulting from contact of irritant materials with the skin.

CLASSIFICATION

What Morrow said with regard to classification thirty-five years ago still holds good at the present time; namely, that "a classification based

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* Read at the Forty-Fifth Annual Meeting of the American Dermatological Association, Washington, D.C., May 2-4, 1922.

1. Morrow, Prince A.: Drug Eruptions, in Selected Monographs on Dermatology, London, The New Sydenham Society, 1893. (The monograph was first published in 1887.)

2. This signification would exclude argyria.—T.Colcott Fox.

upon the anatomical form of the lesions produced by drugs is impracticable. The very multiformity of the lesions forbids any such attempt, for while the irritant action of a particular drug may, in one individual, be manifested by a single elementary lesion, the same drug may produce, in another individual, eruptive elements of dissimilar forms."

CERTAIN PHASES OF THE SUBJECT OMITTED

References to certain phases of the subject are omitted in this paper. Among these are:

1. Combined eruptions of dermatitis medicamentosa and dermatitis venenata, such as occur after the application of a belladonna plaster, absorption through the skin resulting in a general toxic rash, together with a local reaction at the site of the plaster, or, a local and general mercurial eruption following the application of blue ointment to a limited area of the skin.

2. Eruptions resulting from the simultaneous employment of more than one remedy, as mercury and arsphenamin, or mercury and potassium iodid. The European literature deals with several recently published articles on this aspect of the subject.[3]

3. Various types of stomatitis, as those provoked by mercury and the arsphenamins.

4. The general constitutional symptoms associated with drug eruptions; for example, malaise or fever, and injury to the viscera.

5. Eruptions occurring at the site of and around the point of injections of certain drugs; for example, arsphenamin necrosis from faulty technic; or, zosteriform skin necrosis after intramuscular injection of mercury succinimid, recently described by Jadassohn [4] and by Saphier.[5]

3. Gutmann, C.: The Treatment of Syphilis with Neo-Arsphenamin-Novasurol (Bruck) and with Neo-Arsphenamin-Cyarsal (Oelze), Berl. klin. Wchnschr. **58**:1233 (Oct. 17) 1921. Menze, H.: Exanthems from Recurrence of Syphilis During Treatment with Arsphenamin and Arsphenamin-Mercury; Influence of Predominant Conditions on the Wassermann Reaction and Allergy, München. med. Wchnschr. **68**:1290 (Oct. 7) 1921. Levin, Ernest: Localized, Recurrent, So-Called Fixed Exanthems After Arsphenamin and Mercury, Dermat. Wchnschr. **72**:278 (April 9) 1921. Gutmann, C.: So-Called Fixed and Generalized Urticarial Recurrent Exanthems After Arsphenamin and Mercury, Dermat. Ztschr. **35**:135 (Dec.) 1921. Mergelsberg, Otto: A Case of Hypersusceptibility Toward Mercury and Silver Arsphenamin, Dermat. Ztschr **31**:129 (Sept.) 1920. Heller, Julius: Further Communications as to the Occurrence of Severe Arsenical Melanosis and Hyperkeratosis After Combined Neo-Arsphenamin and Mercuric Salicylate Treatment, Arch. f. Dermat. u. Syph. **130**:309 (March 31) 1921; Berl. klin. Wchnschr. No. 46, 1918.

4. Jadassohn, J.: Zosteriform Skin Necrosis After Intramuscular Injections of Mercuric Succinimid, München. med. Wchnschr. **68**:852 (July 8) 1921.

5. Saphier, J.: Zosteriform Skin Necrosis After Intramuscular Injections of Mercuric Succinate, München. med. Wchnschr. **68**:394 (April 1) 1921; Another Case of Zosteriform Skin Necrosis After Intramuscular Injections of Mercuric Succinimid, ibid. **68**:990 (Aug. 5) 1921.

DRUG ERUPTIONS FROM THE NEW ARSENICAL PREPARATIONS (ARSPHENAMIN, NEO-ARSPHENAMIN, SILVER ARSPHENAMIN, ETC.)

From the clinician's point of view, the different eruptive phenomena provoked by the arsphenamin compounds are of considerable interest. Certain phases of the subject may be arbitrarily itemized as follows:

1. Attempts to classify types of eruptions.

2. Occurrence of peculiar forms of eruption. Among these are the so-called "fixed" eruptions, analogous to those following antipyrin and phenolphthalein administration. Lichenoid and lichen planus-like dermatoses, and even true lichen planus, are included under this heading. In the literature are found articles describing posteruptive manifestations under the titles of pemphigus foliaceus, hemorrhagic purpura, leukomelanoderma, Raynaud's syndrome, stomatitis, aplastic anemia and so forth.

3. Occurrence of the ordinary arsenic eruptions from the use of arsphenamin. Among these are dermatitis exfoliativa, hyperkeratoses, palmar and plantar keratodermas, pigmentations, erythemas and so forth; herpes zoster.

4. Argyria from silver preparations.

5. The influence of arsphenamin eruptions on the course of syphilis; "esophylaxis," a term applied by E. Hoffman to a phenomenon involving the reversal of a positive to a negative Wassermann reaction, after a severe arsphenamin eruption.

ATTEMPTS AT CLASSIFYING TYPES OF ERUPTIONS

A classification of the different eruptions provoked by the arsphenamins presents the same difficulties that are encountered in trying to classify the eruptions from arsenic itself. The whole gamut of cutaneous lesions, from faint erythema to squamous-cell cancer, from mild freckling to deep-seated melanoderma, is included under the term arsenical dermatitis. Arsenical zoster also comes under this heading.

Stühmer [6] classifies arsphenamin dermatitis under three headings: (1) acute vasotoxic arsphenamin dermatitis; (2) subacute, anaphylactoid arsphenamin dermatitis, and (3) chronic arsphenamin dermatitis. The last is divided into early and late forms.

The acute vasotoxic dermatitis appears immediately, or within a few hours, or at most within one or two days after the injection. Included in this group are the eruptions appearing within this lapse of time, consisting of acute urticarial and erythematous rashes, as well as those limited to certain parts of the body and called "fixed" arsphenamin

6. Stühmer, A.: Arsphenamin Exanthems; Attempt at Classification; Practical Important Peculiarities of Chronic Arsphenamin Dermatitis, Dermat. Ztschr. **34**:304 (Oct.) 1921.

eruptions. In this type of eruption, Stühmer assumes that, for some unknown reason, there exists in certain areas of the skin a hypersusceptibility against arsphenamin oxids. He believes that these oxids are present to a greater or less extent even in the best preparations of arsphenamin. In this connection, he speaks of a so-called "oxid-reaction." This may be primary, resulting from oxid formation in vivo, or secondary resulting from oxid formation in vitro. He believes that arsphenamin in the body may undergo oxidation and may be synthetized into an albuminous compound through a reaction produced by combination with normal serum. He believes that these various reactions result from a reaction toward the "oxid-protein-body" which is produced in this manner, and which he calls "oxid-toxin."

The subacute, anaphylactoid dermatitis appears from six to twelve days after the first injection of arsphenamin. The second and third injections have no bearing on the causation of the eruption, even though it becomes manifest at the time of the second or third treatment. It is characterized chiefly by the fact of its appearance after the first injection. The author believes this form of reaction to be analogous to serum sickness, which it resembles with respect to the localization of the rash, the temperature curve, the time interval after the first injection, and the fact that subsequent treatments may be administered without harm, after the subsidence of the reaction. Included in this group are the recurrent exanthems described by Nathan. In these, the rash appears from ten to fourteen days after the first injection, fades within a few days to a great extent, and then may partially recur. In this type, also, he found that it is safe to administer further treatment after the subsidence of the rash.

Chronic dermatitis is divided into early and late forms. The early form manifests itself at the termination of a course, after the fifth or sixth treatment; the late form, from several weeks to two or three months after the completion of a course of injections. These eruptions represent the severest types of dermatitis, often beginning as harmless looking follicular, urticarial or erythematous rashes on the extensor surfaces of the extremities. These soon may develop into a generalized dermatitis, going on to the characteristic erythroderma. With the continuation of the process, severe desquamation sets in, following which there may be the formation of hyperkeratoses, and marked changes in the hair and nails, together with pyodermic manifestations, the whole process presenting a severe and serious affection. Sometimes the eruption presents large plaques of weeping dermatitis with extensive areas of desquamation; there may be high fever, and the patient may die. This clinical course may obtain in both the early and the late forms; in the late form, however, the patient would seem to have withstood the

ill effects of the drug, having no reaction whatever until several weeks have elapsed; then suddenly, and without apparent cause, the reaction sets in. Stühmer lays emphasis on a clinical feature of the chronic form of dermatitis which he considers of importance from the therapeutic standpoint; namely, the fact that after the partial subsidence of the acute eruption, the persistent erythroderma remains longest and is most severe in the areas of predilection to seborrheic dermatitis. He believes that patients with seborrheic skins are more susceptible to arsphenamin dermatitis.

Moore and Keidel [7] published a comprehensive paper on arsphenamin reactions, part of which goes into the subject of classification. They differentiate a mild and a severe group of reactions on the basis of their constitutional manifestations and their significance as regards the further treatment of syphilis. Urticaria, erythema and herpes comprise the mild group; mascular, maculopapular and exfoliative rashes, itching and stomatitis, the severe group.

Thirty-one reactions were observed in their series of twenty-three patients. Urticaria was seen six times, erythema once, herpes simplex twice, macular or maculopapular rashes five times, exfoliative dermatitis fourteen times, stomatitis twice, and itching once. The authors regard the macular and maculopapular rashes, the vesicular eruptions and exfoliative dermatitis as degrees of the same process. The rash "begins as a maculopapular or vesicular dermatitis, often limited to the extensor surfaces of the limbs, but rapidly spreading until the whole body is involved. In the milder cases, particularly of the macular or maculopapular type, the process may stop with this, and the eruption disappear in a few days. Frequently, there is a late fine branny exfoliation. In the more severe maculopapular, and especially the vesicular eruptions, marked scaling and exfoliation usually takes place, and the skin of the entire body is desquamated in large flakes. Often an entire palmar or plantar surface comes away intact. The rash is accompanied by the most intense and distressing itching. Usually, the exfoliation is complete in from three to four weeks, but in some cases healing may take much longer. Once or twice, it has been noted that several distinct exacerbations have occurred in the same patient, the skin continuing to exfoliate periodically for several months." Conjunctivitis, involvement of the buccal surfaces, with swelling and denudation of the tongue and buccal mucosae, may also occur.

Brauer [8] recognizes two groups of reactions, primary and secondary.

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7. Moore, J. E., and Keidel, A.: Dermatitis and Allied Reactions Following the Arsenical Treatment of Syphilis, Arch. Int. Med. **27**:716 (June) 1921.

8. Brauer, A.: Contribution to the Subject of Arsphenamin Dermatoses, Dermat. Ztschr. **19**:800, 1912.

In the primary group, he includes the "genuine toxic exanthems," of which he saw sixteen instances in thirteen of 1,500 patients; nine were erythematous, scarlatiniform or morbilliform, with or without stomatitis; one was erythemato-urticarial, complicated by edema; two were exudative erythema multiforme; one was purpura rheumatica with erythema nodosum; and one was severe universal pemphigoid dermatitis. As secondary dermatoses, he classes herpes simplex and zoster, hyperhidrosis, alopecia, alterations in the nails, jaundice, melanoses following primary rashes and immediate macular and urticarial eruptions. He does not believe that these reactions are due to the actual toxic effect of the arsenic; the Herxheimer reaction is considered to be directly related to the urticarial eruptions, which are due to the destruction of foci of spirochetes in the skin.

THE SO-CALLED "FIXED" ARSPHENAMIN ERUPTIONS

On rare occasions, arsphenamin provokes so-called "fixed" eruptions. These are very much like those seen in persons susceptible to antipyrin and phenolphthalein. They consist of from one or more to several dozen sharply circumscribed, slightly elevated, smooth plaques, which may be pink, red, yellowish or brown; sometimes they leave no trace, at other times a moderate grade of pigmentation. They have a tendency to disappear in the intervals between the injections, only to reappear in situ after each administration of arsphenamin. Such cases were first described by German authors (Naegeli, Bitterling, Engwer and Josephson, Fuchs, Grütz, Hecht, Hofmann, Kraus, E. Levin, Nathan, Schoenfeld, Stern), and in one article by the French authors Thibierge and Mercier. More recent papers on the subject have been published by Leibkind, Süring and Gutmann.[9] Drs. Goldenberg and Chargin presented a patient with such a "fixed" arsphenamin eruption, before the New York Academy of Medicine, at one of last year's meetings of the section on dermatology. In this patient, a man, there were two or three well-defined, pink, elevated, round plaques on the thighs and trunk, from one-half to three-quarters inch (1.2 to 1.8 cm.) in diameter. They appeared shortly after an injection of arsphenamin, vanishing in the intervals between treatments. They closely resembled the plaques of an antipyrin rash. In a general way, this type of eruption simulates the fixed types of antipyrin and phenolphthalein dermatoses. As has been stated elsewhere,[10] those who have the

9. Gutmann, C.: Concerning So-Called "Fixed" and Generalized Urticarial Relapsing Exanthems After Arsphenamin and Mercury, Dermat. Ztschr. **35**:135 (Dec.) 1921. (This article furnishes references to the literature of "fixed" arsenical eruptions).

10. Wise, Fred, and Abramowitz, E. W.: Phenolphthalein Eruptions, Arch. Dermat. & Syph. **5**:297 (March) 1922.

opportunity to investigate this peculiar recurring and relapsing dermatosis must always bear in mind the possibility that the patient is taking either antipyrin or one of the numerous phenolphthalein preparations while undergoing his course of arsphenamin injections. The point of special interest in these "fixed" arsphenamin rashes lies in the fact that the lesions tend to relapse and to recur in situ, and to flare up quite markedly after each injection, to fade partly, with or without leaving pigmentation, in the intervals between injections, or to vanish entirely, without leaving a trace.

LICHENOID ERUPTIONS

Mention of lichenoid, lichen planus-like and apparently genuine lichen planus eruptions are found in the literature on arsenical dermatoses preceding the arsphenamin era. Brooke and Roberts,[11] in their paper on the British arsenical beer-poisoning epidemic, speak of rather frequent lichen planus-like rashes. Recently, several European publications have appeared dealing with lichenoid and lichen planus post-arsphenamin eruptions. Eruptions resembling lichen planus are reported by Kleeberg,[12] Buschke and Freymann,[13] Keller [14] and others.

Most of these accounts state that there is a "striking similarity," both clinically and microscopically, to lichen planus. Naturally, the pros and cons of the question as to whether the arsphenamin "lights up" a latent lichen planus in a patient subject to the disease, or whether the drug actually causes an eruption of lichen planus, are discussed by the various reporters. Buschke and Freymann content themselves by invoking the homeopathic dictum: Similia similibus curantur. Keller reports a case which in his estimation is an undoubted lichen planus, both clinically and histologically. Queyrat, Louis and Rabut [15] report a patient who suffered from recurring plaques of erythema of the body, associated with a lichen planus eruption of the tongue; Civatte pronounced a microscopic section from one of the tongue lesions true lichen

11. Brooke, H. G., and Roberts, Leslie: The Action of Arsenic on the Skin as Observed in the Recent Epidemic of Arsenical Beer Poisoning, Brit. J. Dermat. **13**:121 (April) 1901.

12. Kleeberg, L.: Clinical Aspects of Arsenical Exanthems, Therap. Halbmonatsh. **35**:370 (June 15) 1921.

13. Buschke, A., and Freymann, W.: Lichen Ruber-Like Arsphenamin Exanthems, Med. Klin. **17**:899 (July 24) 1921; Further Contribution to Lichen Ruber-Like Exanthem After Arsphenamin, Dermat. Wchnschr. **73**:945 (Sept. 10) 1921.

14. Keller, P.: Lichen Planus and Lichenoid Arsenical Dermatitis, Dermat. Wchnschr. **74**:9 (Jan. 7) 1922.

15. Queyrat, Louis and Rabut: Lichen Planus of the Tongue Appearing in a Syphilitic During the Course of an Arsenic Treatment, Together with Generalized Erythema Following Arsenical Injections, and Leaving Plaques of Pigmentation, Bull. Soc. franç. de dermat. et syph. 1921, No. 2, p. 39.

planus. In the discussion, Milian said that he believed that the arsenic injection provoked an exacerbation of a preexisting or latent lichen planus, while Thibierge contradicted him, saying he did not think that such an explanation was plausible.

Recently, one of our colleagues at the Vanderbilt Clinic, Dr. McCafferty, brought to us a patient from his service at the Presbyterian Hospital, in whom a lichen planus eruption, confirmed by microscopic examination, appeared after a course of arsphenamin and mercury injections. As Dr. McCafferty intends to report this case fully, a detailed account is omitted here. The patient was a negress, aged 40, with active syphilitic cutaneous lesions and atrophic scarring from preexisting eruptions. The Wassermann reaction was strongly positive. She received ten or twelve injections of arsphenamin and mercury, at weekly intervals. Toward the end of this course of treatment, a widespread lichen planus eruption appeared, being most pronounced on the trunk and extremities, while the lingual and buccal mucosae exhibited slightly elevated grayish plaques. The exanthem was associated with severe pruritus. She had never had an attack of lichen planus.

Among other unusual cutaneous reactions may be mentioned a case of hemorrhagic purpura, reported by Anwyl-Davies,[16] following injections of neo-arsphenamin. Deep melanosis and hyperkeratosis are reported by Nördlinger,[17] and by Heller [18] and others. Nicolas, Massia and Dupasquier [19] describe a patient with Raynaud's syndrome with gangrene, after neo-arsphenamin injections. A case of pemphigus foliaceus following the administration of the same preparation is reported by Nicolas and Massia.[20] Moore and Keidel [21] published a paper on stomatitis and aplastic anemia following arsphenamin treatment of syphilis. The literature on dermatitis exfoliativa and on icterus is abundant.

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16. Anwyl-Davies, T.: Hemorrhagic Purpura Following the Therapeutic Administration of Neo-Arsphenamin, Brit. J. Dermat. & Syph. **33**:264 (July) 1921.

17. Nördlinger, A.: A Case of Deep Melanosis and Hyperkeratosis, Arch. f. Dermat. u. Syph. **131**:257 (April 30) 1921.

18. Heller, J.: Further Contribution on the Occurrence of Severe Arsenical Melanosis and Hyperkeratosis After Combined Neo-Arsphenamin and Mercuric Salicylate Treatment, Arch. f. Dermat. u. Syph. **130**:309 (March 31) 1921.

19. Nicolas, J., Massia, G., and Dupasquier, D.: Raynaud's Syndrome with Gangrene, of Neo-Arsphenamin Origin, Ann. de dermat. et syph. **2**:193 (May) 1921.

20. Nicolas, J., and Massia, G.: A Contribution to the Study of Arsenobenzolids; Pemphigus Foliaceus due to Arsenobenzol, Ann. de dermat. et syph. **2**:145 (April 1921.

21. Moore, J. E., and Keidel, Albert: Stomatitis and Aplastic Anemia Due to Neoarsphenamin Treatment, Arch. Dermat. & Syph. **4**:169 (Aug.) 1921.

ORDINARY ARSENIC ERUPTIONS

In the early period of arsphenamin treatment, it was thought by many clinicians that the new arsenical preparations were not prone to give rise to the characteristic arsenical dermatoses which have always been associated with the prolonged use of the old arsenicals; namely, keratoses, palmar and plantar hyperkeratoses and melanoses. As time went on, case reports began to crop out here and there, so that the literature of the day contains a fairly large number of instances illustrating the hyperkeratotic and pigmentary by-effects in the skin of susceptible persons who had never taken arsenic, but who had received arsphenamin for syphilis. Among other writers, Heller [22] published two good articles on this phase of the subject. He reported three cases in which severe melanosis and hyperkeratosis occurred after combined neo-arsphenamin and mercuric salicylate treatment. After the publication of this report, he observed five similar cases in connection with the same combined treatment. Two of the patients had a cutaneous inflammation, without melanosis or hyperkeratosis. In two other patients, an intensive melanosis developed; in one, only hyperkeratosis. The last mentioned patient died so early that it was not possible to observe the melanosis. Six of the first described cases presented typical changes in the skin. None of the six showed any signs of idiosyncrasy in the beginning of the treatment, and in all the skin disease appeared toward the end of the treatment. None of them showed any signs of irritability toward mercury. Palmar and plantar hyperkeratoses were observed in all of the six patients. The anomaly of cornification was exhibited in Patients 3, 4, 5 and 6; the melanosis in Patients 1, 2, 4 and 6. Patient 5 died before the period in which the melanosis usually manifests itself. A striking example of palmar and plantar keratoderma is described and illustrated by Edmund Hofmann,[23] who also refers to the case reports of Heller,[22] Philip [24] and Pürckhauer.[25]

Herpes simplex and herpes zoster are comparatively frequent cutaneous manifestations following arsphenamin treatment. As to the

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22. Heller, Julius: Further Communication as to the Occurrence of Severe Arsenical Melanosis and Hyperkeratosis After Combined Neo-Arsphenamin and Mercuric Salicylate Treatment, Arch. f. Dermat. u. Syph. **130**:309 (March 31) 1921; idem, Berl. klin. Wchnschr. **46**, 1918.

23. Hofmann, Edmund: Concerning Arsphenamin Exanthems, Dermat. Ztschr. **31**:1 (July) 1920.

24. Philip, Caesar: Arsenic Keratoses After Arsphenamin Injections, München. med. Wchnschr., 1915.

25. Pürckhauer: Arsphenamin Intoxication Running a Course with Fever and Dermatitis Exfoliativa, Developing into Arsenomelanosis and Arsenical Hyperkeratosis, München. med. Wchnschr. 30, 1917.

occurrence of malignant changes which are sometimes encountered in connection with arsenical keratoses, we have not as yet run across such a reference in the literature.

ARGYRIA FROM SILVER ARSPHENAMINS

No authentic case of postarsphenamin argyria has been recorded. Schlossberger's [26] report was based on hearsay evidence only.

THE INFLUENCE OF ARSPHENAMIN ERUPTIONS ON THE COURSE OF SYPHILIS: "ESOPHYLAXIS"

Erich Hoffmann [27] applied the term "esophylaxis" to a phenomenon observed in certain patients with severe arsphenamin reactions. In these patients, it was discovered that a strongly positive Wassermann reaction would become negative after an attack of arsphenamin dermatitis and would remain negative for a long time thereafter. Corroborative testimony to this effect has been offered by Buschke and Freymann,[28] Carl Bruck,[29] S. Levi [30] and F. Lesser.[31] The last named writer takes up the question in detail, stating that it could be proved only by the collection of statistics extending over at least two years.

Statistics as to the effect of mercury treatment and of insufficient treatment of tabes are not satisfactory, since they are not uniform. A comparison must be made between syphilitic patients who have had identical treatment and have been observed for the similar periods of time, to determine whether those with drug eruptions have had fewer clinical and serologic recurrences. Lesser discusses the theory that the skin has a defense reaction which protects the internal organs from the disease, which Hoffmann calls esophylaxis. This theory is supported by the fact that syphilitic persons who have had intense skin eruptions and frequent recurrences in the early stages have tabes and paresis more rarely than those who have had slight skin eruptions. Lesser's explanation of this is as follows: While the skin symptoms are visible,

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26. Schlossberger, H.: Supposed Case of Argyria After Silver Arsphenamin, Therap. Halbmonatsh. **34**:608 (Nov.) 1920.

27. Hoffmann, Erich: Late Exanthems after Arsphenamin, Niederrh. Ges. f. Nat. u. Heilk., Med. Abt., Feb. 20, 1911; Abstr. Deutsch. med. Wchnschr., 1911, p. 2058.

28. Buschke, A., and Freymann, W.: Influence of Arsphenamin Exanthems on the Course of Syphilis, Berl. klin. Wchnschr., 1921, No. 15.

29. Bruck, Carl: Influence of Arsphenamin Exanthems on the Course of Syphilis, Berl. klin. Wchnschr. **58**:518, No. 20, 1921.

30. Levi, S.: Syphilis Following Toxic Exanthems, Berl. klin. Wchnschr. **58**:1137 (Sept. 19) 1921.

31. Lesser, Fritz: The Effect of Toxic Exanthems on the Course of Syphilis, Berl. klin. Wchnschr. **58**:1210 (Oct. 10) 1921.

those in the internal organs are latent, as is shown by the positive findings in the cerebrospinal fluid at the time of the eruption. As the cell infiltration in the early stage is a defense reaction against the spirochetes, it is to be assumed that such defense reactions are also taking place in the internal organs. This pronounced organic immunity will frequently bring about a cure of the syphilis, and if not, will protect the organs from late syphilis. Milder skin symptoms indicate weaker defense reactions, a lesser degree of immunity, more frequent recovery and more frequent late syphilis. Arguments against esophylaxis are furnished by the positive cerebrospinal fluid findings in the early period, the fact that the disease can be reproduced by inoculations with the cerebrospinal fluid with a negative blood Wassermann reaction, and the possibility of experimental inoculation with all the internal organs. Buschke and Freymann's assertions that slight erythemas have no effect, and only eczematoid eruptions with pronounced skin changes have any effect, are in contradiction to the usual findings that changes in the skin decrease the function of the organs. But the high fever which precedes or accompanies the exanthem may have a favorable effect on the course of the syphilis. The chronicity of syphilis may be due to its afebrile course.

A criticism of the opinion that syphilis is favorably influenced by arsphenamin eruptions is expressed by Benveniste.[32] Five examples are briefly reported which show that, although erythroderma coincides with the disappearance of the positive Wassermann reactions, this effect is only transitory, lasting but a few months; and usually a clinical relapse is observed when the Wassermann reaction becomes again positive. No beneficial influence is, therefore, to be attributed to the exanthems produced by arsphenamin. On the contrary, in view of the fact that arsenic cannot be used further, the prognosis becomes less favorable in these cases.

Another French author, Gougerot,[33] cites several examples favoring the theory of so-called "esophylaxis." He thinks that the explanation of the reversal of a positive to a negative Wassermann reaction, after the appearance of a toxic exanthem, may be referred to the assumption that the tissues have been more strongly impregnated with the drug than usual, that arsenic is retained in the body, or again that the fever which sometimes accompanies arsenical erythroderma has had a destructive effect on the spirochetes. It has also been suggested that

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32. Benveniste, Elie: Exanthems Produced by Arsphenamin and the Evolution of Syphilis, Presse méd. **29**:904 (Nov. 12) 1921.

33. Gougerot, M.: Syphilitic Relapse with Visceral, Cutaneous, Mucous and Serologic Manifestations Soon After an Exfoliating Erythroderma, Consecutive to Treatment with Arsphenamin, Bull. et mém. Soc. méd. d. hôp. de Paris **37**: 1339 (Oct. 27) 1921.

the violent cutaneous reaction may cause "the production of defensive substances by the skin, which help the action of specific therapy." In his article, Gougerot mentions a series of cases in which the toxic eruptions produced a favorable reversal of the Wassermann reaction. But, in contrast to these, he also cites several examples in which no such reversal of the serologic findings took place. In one patient, there was a relapse within two months after the appearance of the toxic rash, with special localization in the nervous system and with the appearance of syphilitic cutaneous papules. In another patient, there was a relapse within two months after the toxic eruption, even before the latter was completely cured.

RECENT SYNTHETIC DRUGS

The large majority of the new synthetic remedies are capable of provoking eruptions in those who are susceptible. These are usually described as erythematous, urticarial, morbilliform, scarlatiniform, erysipelatous, bullous, erosive and so forth. It is probable that a great many of these eruptions, being ephemeral and causing no inconvenience to the patient, never come to the physician's notice. Simulating the acute exanthems, as many of them do, these eruptions are naturally of interest to both the dermatologist and the general practitioner. Scattered references are frequently encountered in the literature, and recently Lutz [34] has published a review of the subject. Among the remedies mentioned in his paper, some of the following are more or less freely prescribed in this country:

Barbital and Medinal (Sodium salts of Diethylbarbituric Acid and Diethylbarbituric Acid). Gregor encountered exanthematous rashes with fever after two or three small doses. The eruptions disappeared as soon as the drugs were withdrawn; renewed administration was followed by a rash more intense than the first. Weitz described a morbilliform, partly confluent itchy eruption and erythematous swelling of the face, with an increase in temperature in a girl, aged 22, who had been taking doses of medinal of unknown quantity. She died two days after the appearance of the rash. Pollitzer found, after barbital administration, a much darker morbilliform rash in a patient who had been taking 1 gm. of the drug every night. The rash was associated with red blotches on the cheeks and pharyngeal mucosa, and with erosions of the mouth and anus. Pernet and Mertens report the appearance of blebs within five minutes after the ingestion of barbital. In another case, the blebs appeared on the third day. They

34. Lutz, Wilhelm: Dermatoses from the Newer Remedies (Excepting Arsenic and Mercury), Therap. Halbmonatsch. **35**:489 (Aug) 1921, and **35**:521, 1921. (This article furnishes references to the literature).

were localized on the external aspect of both forearms, their contents were cloudy, and they had no areolae. Localized, so-called "fixed" eruptions are described by Klausner, Zeisler, Glaser and Lichtenstein.

Codeonal (Codein-Barbital). Beyerhaus saw a patient develop bluish-red, severely itching plaques on the face and chest, later extending over the entire body, and associated with fever, within three hours after taking 0.18 gm. of the proprietary codeonal. It is not known whether these untoward effects were due to codein, as Beyerhaus seems to think, or to the barbital.

Adalin and Bromural (Bromidethylacetylcarbamid and Monobromisovalerylurea): In three cases, Fürbringer saw, on the day following the administration of adalin, an intense pruritus, and in a fourth patient, an attack of itching with urticaria which lasted twenty-four hours. Roeder saw similar cases. Walter met with a bromid acne as an untoward effect of adalin. Zetlin and Giorgio saw a pustular and tuberose bromid dermatitis after administration of bromural—a drug belonging to the same group as adalin. Loeb [35] reported six cases of adalin eruption. These appeared partly in the form of papular eczematoid eruptions of either the acute or the chronic variety, partly as erythematous, irregularly outlined, more or less edematous and infiltrated plaques, which showed some similarity to long standing forms of exudative erythema. Petechiae and telangiectases were noted in one case. Pigmentation may remain after the lesions subside. One patient had urticaria of the face. The eruption appeared in irregular, geographic outlines, with no tendency to coalescence. The sites were chiefly on areas subject to pressure from the clothing, or where the skin was irritated. The eruptions were symmetrical, and the mucosae were not involved. Pruritus was marked during the night; less troublesome during the day. The drug was given experimentally and produced the same eruption. In two patients, a long time intervened before the second administration of the drug. There was no rise of temperature. The eruption faded in about two weeks without leaving a trace, except mild pigmentation. Old people seem to be more susceptible.

Phenobarbital (Phenylethylbarbituric Acid): A universal erythema in two patients is mentioned by Gräfner; and a rubeolar rash on the chest, back, arms and thighs, with a red swelling of the face, disappearing at the end of a week with desquamation, by Fröderstrom. Several authors reported morbilliform eruptions. Juliusburger, Fürbinger, Haug and Emanuel describe a scarlatiniform exanthem. Several eruptions, some resembling measles and some scarlet fever, were seen by Strauss in five patients. In two of them, the rash appeared within a few days after taking doses of 0.05 gm. two or three times a day.

35. Loeb, H.: Concerning an Exanthem from Adalin, Arch. f. Derm. u. Syph. **131**:128 (April 30) 1921.

Luce and Feigel had a similar experience. In their cases, however, the rash was accompanied by a hyperemia of the conjunctivae, mouth and pharyngeal mucosae; in two instances, the fever was high, and, after four to seven days, disappeared, with desquamation. Konig and Meissner cite similar cases. Raecke saw one patient with an urticarial eruption. Curschmann saw three patients with eczematous eruptions and dermatitis. Exanthems which cannot be classified are described by Loewe, Zimmermann, Moerchen and Blickert. Fürer, König and Juliusburger, twelve hours after a subcutaneous injection of this drug saw a pea-size blister develop at the site of the injection. In one case, necrosis occurred. No such complications followed injections into the subcutaneous fatty tissue. Phenobarbital eruptions are frequently associated with lingual and oral erosions. At one of the recent meetings of the section on dermatology of the New York Academy of Medicine, Chargin presented a remarkable case of pemphigoid erosion of the entire tongue, in an epileptic girl who had been taking phenobarbital, and who had no cutaneous rash. These tongue and mouth eruptions closely simulate antipyrin and phenolphthalein erosions. Phillips [36] reports a case of severe poisoning from phenobarbital, accompanied by an extensive erythematous and morbilliform eruption, which itched severely, and swelling of the oral mucosae. This paper also describes a number of other cases previously reported.

Cinchophen (Phenylquinolincarboxylic Acid): After the use of this drug, Stiefler reports angioneurotic edema. Maranon saw an erysipelatous swelling of the face with chills, on two occasions, in one patient; thereafter, the drug was well borne. He also reports an intense pruritus in a patient who for months before had been taking the drug without any ill effects. Scarlatiniform, urticarial and mixed rashes are also reported. Oyarzabal saw a patient in whom an eczema on the back of the neck, previously induced by formaldehyd, was aggravated by the subsequent administration of atophan. Fricke saw herpes zoster make its appearance while the patient was under the influence of the same drug.

Pyramidon (Dimethylaminoantipyrin): Scherber and Weidenfeld report a case in which a single dose was followed by the appearance of two concentric, red, elevated circles on the left cheek. In a patient who had previously borne antifebrin well, Bechet observed the development of a large swelling of the lower lip and a severe pruritus of the face and neck, with an erythematopapular and partially urticarial exanthem with petechiae on the feet and legs. This rash appeared after the patient had taken pyramidon daily for four days. It disappeared entirely after three days.

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36. Phillips, John: Phenobarbital (Luminal) Poisoning, J. A. M. A. **78**:1199 (April 22) 1922.

Melubrin (Sodium salt of Antipyrinamidomethansulfonic Acid): Krabbel reports an exanthem associated with this drug similar to that following antipyrin. Mullers had a patient who, after taking 0.5 gm. acetysalicylic acid daily, developed a few small papules on the arms. After the acetysalicylic acid was replaced by melubrin (2 gm. daily) there followed, two days later, an aggravation and extension of the rash. It extended over the entire body, and became coarser and itchy.

Acetylsalicylic Acid: The eruptions described following acetylsalicylic acid ingestion are comparatively uniform. In some cases, within an hour, swelling of the face, chiefly of the eyelids and lips appears, generally accompanied by swelling of the nasal, buccal and pharyngeal mucosae, frequently with intense general malaise. Some patients develop urticaria, others a scarlatiniform rash, and still others conjunctivitis with edema of the eyelids. Kraus saw two cases of "dyshidrotic eczema" following the use of the drug.

Hexamethylenamin: Hilbert reports the case of a woman, who, immediately after taking a tablespoonful of a 5 per cent. solution, developed an intense itching and burning eruption over the body; half an hour later, after a second dose, there appeared swelling of the eyelids, redness of the conjunctivae, and urticarial wheals the size of lentils, all over the trunk and scalp. Sachs reports a similar experience; in his case, headache, tinnitus, a temperature of 40 C., and a light red efflorescence on the trunk also developed.

Phenolphthalein: Eruptions from phenolphthalein were described in detail at last year's meeting of this Association.[10] Since then, several new examples of the eruption have been presented before various medical societies, and three articles on the subject have been published; one by Ayres,[37] dealing with the exanthem itself, another by Corson and Sidlick,[38] who report urticaria from the habitual use of the drug, and another by Rosenbloom,[39] who records a case of nasal herpes which always recurred after the patient took a proprietary phenolphthalein pill.

DISCUSSION

ON PAPERS OF DRS. WILE, WRIGHT AND SMITH, AND WISE AND PARKHURST

DR. JOHN H. STOKES, Rochester, Minn.: I am sure I voice the sentiment of the Association when I say that to have heard these papers makes the trip to Washington very much more than worth while. I believe that the essayists deserve a unanimous vote of thanks for such a splendid presentation of such

37. Ayres, Samuel: Phenolphthalein Dermatitis, J. A. M. A. **77**:1722 (Nov. 26) 1921.

38. Corson, Edward F., and Sidlick, D. M.: Urticaria from Habitual Use of Phenolphthalein: Report of a Case, J. A. M. A. **78**:882 (March 25) 1922.

39. Rosenbloom, Jacob: Report of a Case of Nasal Herpes Due to Ingestion of Phenolphthalein, J. A. M. A. **78**:967 (April 1) 1922.

an intricate subject. It occurred to me that I might add something to the interest of the evening if I mentioned one or two of the observations made on our service by Dr. E. D. Osborne, who has been studying the chemical aspects of iodid administration.

Reactions to sodium iodid administered intravenously in doses ranging from 2.5 to 20 gm. a day are relatively rare. Patients who show pronounced reactions to potassium iodid by mouth tolerate sodium iodid intravenously without incident. Such reactions as occur are practically all of an anaphylactic type, including urticaria, erythema multiforme and local edemas of the eyelids and the larynx. Transient asthmatic symptoms may develop. If iodid acne develops, it is usually mild. We have seen no fungoid or bullous lesions. Dr. Wise mentioned the slow elimination of the bromids and the cumulative action. There is no cumulative action in the administration of iodid regardless of the method of administration or the dose. The drug has completely left the body within seventy-two hours after administration. Not over 5 per cent. of the iodid is eliminated in the stools. Practically all of it leaves the body through the kidneys.

In investigating the possible dissimilarities in action in the case of sodium and potassium iodids, Dr. Osborne made several interesting observations. Following the administration of sodium iodid by mouth there was a definite marked rise of the sodium content of the blood serum proportional to the size of the dose, with no change in the potassium content. In contrast to this finding, administration of potassium iodid by mouth did not produce a corresponding rise in the potassium content of the blood serum, but, on the contrary, a definite rise in the sodium content almost equal to that following the sodium iodid.

There is no special advantage in giving small doses intravenously. Administration by mouth creates a moderate sustained concentration. Intravenous administration of large doses creates peaks of high concentration followed by rapid decline. Only traces of iodin can be found in the serum proteins after the administration of sodium iodid by mouth. In direct contrast to this finding, from 7 to 26 per cent. of the iodin following the administration of potassium iodid by mouth was found in the serum proteins. Following intravenous administration of sodium iodid, from 6 to 9.9 per cent. of the iodin is found in the serum proteins.

Evidently an exchange of ions occurs in the process of absorption of potassium iodid. The potassium is replaced by sodium to a large extent. Whether in this exchange of ions the iodin from potassium iodid (I am now merely serving as a mouthpiece for Dr. Osborne) is absorbed in the same form as after sodium iodid, is open to question. Since the potassium is evidently absorbed to a very slight degree, the question naturally arises as to whether the iodin after potassium iodid unites with the protein, the fat or the inorganic constituents of the blood. Dr. Osborne's investigations suggest that the iodin in the form of potassium iodid by mouth forms a sodium protein combination while in the case of sodium iodid by mouth only traces of iodin enter into combination with the proteins. In a study not yet completed of two patients showing symptoms of iodism following the administration of sodium iodid by mouth, it was found that the iodin unites with the protein fraction to a greater extent than in normal persons. If iodin when administered in the form of potassium iodid unites with the serum proteins to a greater extent than when administered as sodium iodid the question at once arises as to whether

this sodium protein iodin combination is the basis of the action of iodids, and an explanation of possible differences in the pharmacologic behavior of the two salts. These points must be made the subject of further study.

Dr. William H. Mook, St. Louis: Our work was done about seventeen years ago under very different circumstances than are possible in a modern hospital. It was done at the city poor-house where the laboratory facilities were crude; consequently, owing to faults of technic, the results of making cultures were negative In the histologic examination of this tissue we were struck by the marked changes in the capillaries surrounding these iodid lesions, and we concluded that there was a toxin in the blood that probably attacked the blood vessels instead of the glands of the skin themselves. Frequently they developed at sites of former traumas, especially of old healed acne lesions.

Dr. Herman Goldenberg, New York: Through my connection with a large general hospital and a close contact of the dermatologic department with the medical and surgical services, I have been able to see a great many drug eruptions, probably a much larger number than the average dermatologist. I do not wish to detain you with the enumeration of such ordinary eruptions as you see following the administration of bromids, acetyl salicylic acid, barbital, antipyrin and other coal-tar products, but I wish to report a few unusual drug manifestations which are not at all or only briefly described in textbooks.

I wish especially to call attention to scarlatiniform or morbilliform eruptions following the administration of digitalis or its derivatives, which I, not infrequently, observe, and similar universal eruptions from the use of hexamethylenamin. On the surgical side the same type of skin lesions is occasionally observed following the application of tincture of iodin over large patches for sterilization or the use of an iodoform gauze packing, not at the site of application, but through absorption from the skin. The type of bromid eruption resembling an erythema nodosum, of which Dr. Wise showed a photograph and stated that it was of rather frequent occurrence, is not universally known or described in textbooks. We see every year from three to six cases, generally located on the lower extremities, but also found elsewhere and anywhere on the body, and usually accompanied by a slight rise of temperature.

In addition, I wish to report briefly a number of cases of mouth lesions, either in connection with or independently of skin manifestations which I have seen in private and hospital practice. One of the cases is that of a phenobarbital eruption which was presented from my service by Dr. Chargin and referred to by Dr. Wise. The patient was a young girl who for a period of over two years had taken phenobarbital in doses of 4½ to 6 grains (0.3 to about 0.5 gm.) a day for epilepsy. The tongue was twice the natural size, raw, beefy and had a number of thin walled blisters, filled with blood. These blisters ruptured spontaneously or on the slightest trauma. The mucous membrane of the lips showed lesions resembling mucous patches and multiple hemorrhagic punctae. On admission to the hospital phenobarbital was withdrawn and at the end of the third week the mouth condition was almost normal. It was then given again, and the same eruption produced. A skin sensitization test for phenobarbital was negative. The urine still showed phenobarbital two and one-half weeks after its administration had been discontinued. The second case was that of a man of 40 years who consulted me for an eruption of the tongue consisting of swelling and numerous round and oval erosions without cutaneous manifestations. They resembled mucous patches so much that for the afternoon of the same day an appointment had been made

by a colleague for an arsphenamin injection. In this case the lesions in the mouth were due to salipyrin. After being informed of the cause of his affection, the patient recollected that a year ago he had had a similar attack due to the same cause.

Another case was that of a woman who had suffered for two years with repeated attacks, beginning with itching of the hands and feet, sneezing and a watery discharge from the nose, and eruption of a bullous character in the groins, vagina, rectum, lips and mouth. The patient had made the rounds of dermatologists and had been put on a strict diet on the basis of skin sensitization tests, without any benefit. This eruption was due to cinchophen. When this drug was discontinued, the lesions promptly healed.

I have seen a similar case, following the administration of cinchophen, in a female patient with an erythematous and hemorrhagic eruption of the hands and fingers and a herpetic and bullous eruption on the roof of the mouth and the tip of the tongue.

A few weeks ago I saw a young girl with a generalized scarlatiniform eruption, after one dose of 1½ grains (0.097 gm.) phenobarbital. Three weeks later, this patient developed a peculiar erythema in the flush area of the face resembling a superficial lupus erythematosus and blebs in the mouth, suggesting a drug eruption. This patient had received two injections of phenolsulphonephthalein to test the renal efficiency. I mention this as a mere suggestion that the eruption may have been due to that drug.

Regarding the fixed arsphenamin eruptions which Dr. Wise mentioned in his paper and of which he said on account of their resemblance to antipyrin or phenolphthalein eruptions that one of these drugs might have been administered, I want to state that this was not the case in my patients. Furthermore, we were not able to produce an eruption in the patient with the arsphenamin eruption by the administration of phenolphthalein nor in the patient with the phenolphthalein eruption by the injection of arsphenamin.

You all remember the patient with the unusual eruption, resembling lichen planus, who was presented at our clinical meeting in Boston last year. The eruption followed the injection of arsphenamin. Drs. Wise, Highman and myself considered the condition lichen planus. Drs. Fordyce and Ormsby strongly contested this view, and proclaimed it an unusual arsphenamin eruption. This case resembled closely the one mentioned by the essayist and I now admit that in my opinion the view of my opponents was correct.

The facts mentioned by Dr. Wile, that bromids replace the chlorids in the body, has induced me for many years to give patients with bromid eruptions either a diet rich in salt or to administer calcium chlorid by mouth.

Dr. C. C. Dennie, Kansas City: I would like to offer a suggestion regarding the chemical end of this proposition. I do not think consideration has been taken of what has been called the solution tension of metal. All metals have a solution tension, and iron has a greater one than copper; therefore, iron replaces copper in solution, and the copper is thrown out. The presence of sodium iodid in the blood when potassium iodid has been given can readily be explained on the basis that potassium has a greater tension than the sodium, and in that case the potassium would replace the sodium in the body cell and one would have the sodium eliminated and the potassium retained. When one gives sodium iodid the sodium will not replace the sodium there because it will have the same tension. It might be conceivable that it is the potassium in the cell combination thus retained that causes the trouble.

DR. JAY FRANK SCHAMBERG, Philadelphia: It must have required a great deal of discriminating judgment on the part of Dr. Wise to give us his excellent digest of the literature on this subject. Dr. Wile's contribution acquires a permanent importance because he eliminates untenable hypotheses and his decisions are based on experimental evidence.

As I understood a reference by Dr. Wise, a writer quoted by him assumes that cases of arsphenamin dermatitis are due to the presence of "arsenoxid" in the drug. Ehrlich early stated that all lots of arsphenamin contained traces of arsenoxid, usually less than 1 per cent. I do not believe that we can incriminate arsenoxid as the cause. In the first place, from the use of 2,000 ampules of the same lot, one or two cases of dermatitis may develop. Second, compounds that have given rise to dermatitis were found by analysis not to contain an excessive amount of arsenoxid. Arsenoxid is both more toxic and more curative than arsphenamin, but there is no evidence that it is the cause of dermatitis.

We do not know the fate of arsphenamin, after it is introduced into the blood stream. We know that it produces rapidly a combination with the blood serum. We have produced in the test tube a combination with blood serum, a substance which we evaporated to solid form and after redissolving injected into animals, with results not differing greatly from those of arsphenamin.

In regard to phenobarbital, this drug has come into use extensively on account of its value in epilepsy; we must familiarize ourselves with the eruptions produced by it in order to be of aid to the practitioner.

I saw a man who had been taking 1½ grains of phenobarbital three times a day for three weeks. He presented an intense morbilliform eruption, with bloodshot eyes, with marked stomatitis and with hundreds of blebs over the trunk and studded profusely over the palms and soles. The case had been diagnosed by the practitioner as measles, but I said that I had never seen measles with such a slight rise in temperature and with numerous blebs. I regarded it as a phenobarbital eruption. I would be interested to know whether other members have seen a similar manifestation.

Barbital is apt to produce eruptions which simulate the exanthems. I am sure that many erroneous diagnoses of scarlet fever are made on account of confusion with drug eruptions. I recall a patient with a scarlatinoid rash and a temperature of 101 F. in whom the diagnosis of scarlet fever was made. We stopped the drug, and the symptoms all disappeared; we resumed the drug and the symptoms reappeared. I think we should determine in all drug eruptions whether a leukocytosis exists because its absence would operate against the diagnosis of scarlet fever. In the latter disease there is virtually always a leukocytosis.

DR. HAROLD N. COLE, Cleveland: Some years ago some German research workers, who were studying drug eruptions to ascertain whether they were due to anaphylaxis, worked with potassium iodid. In 1910 I checked up this work. I withdrew some of the blood from patients with acute potassium iodid eruptions, injected the serum into guinea-pigs, and then gave some of the drug to the pigs. We could not confirm the work of the Germans. The same was also true in regard to copaiba eruptions.

DR. SIGMUND POLLITZER, New York: I am very much interested in this subject, but it is of such tremendous scope that it is impossible in the few minutes allowed for discussion to touch more than a few points.

It seems that we have at least two definite classes of effects in drug eruptions. First, it seems certain that the effect of arsenic on the epidermal struc-

ture is something entirely different from the effect produced by any other cutaneous irritant conveyed by the blood. Arsenic exercises a direct influence on the process of cornification. It is on the stimulation of this process that one of the therapeutic uses of arsenic is based. It needs only a slight overstimulation of this cornification to produce the keratoses of arsenic.

With regard to the arsenic in certain organic compounds, it has effects of an entirely different class, presenting a group of symptoms of the erythema multiforme type of eruption. All of the new drugs, I think I am safe in saying all, produce eruptions of the erythema multiforme type—simple erythema, urticaria or scarlatiniform, morbilliform or purpuric eruptions; all of these are simply stages of the same process, which predicates an injury to the blood vessels.

As to the question of iodids and bromids, I remember the interest aroused by Adamkiewicz' announcement of the discovery of iodin in the pustules of iodid acne. It was soon pointed out, however, that the mere presence of iodin in these lesions proved nothing unless it could be proved that there was more in the lesions than elsewhere in the tissues, and of course such a quantitative demonstration was out of the question. Soon after that a number of observers —Duckworth, Thin, Ducrey, and others—showed that it was not true that the pathogenic process began in the sebaceous glands, but that it started in the epidermis over the papillae, and that the involvement of the sebaceous glands was secondary.

With all that has been said, we cannot get away from the fact that a drug eruption depends on something more than the drug. Most people may take these drugs without manifesting any cutaneous effects; there is always the drug plus the patient. That peculiarity in the patient we have been in the habit of speaking of as idiosyncrasy. I have no doubt the time will come when the meaning of idiosyncrasy will be understood, and we will know that it is, after all, a chemical process; but at the present time the nature of this is not understood, and notwithstanding the large amount of work accumulated and the excellent observations presented to us this evening, we do not yet understand it. The pathogenic process in these ills is still a mystery.

Dr. Charles J. White, Boston: In regard to the relation of bromids, I wish to relate this rather extraordinary experience. I was asked to treat an ulcer on the leg of a woman with a remarkably clear white skin. There was no hair and there were no varicose veins. The ulcer seemed remarkable. I asked many questions but received no answers of any value. I tried to heal this ulcer in various ways without success. I tried liquor ferri et potassii tartratis, scarlet red, a fuchsin paste solution, and finally applied surgical solution of chlorinated soda. The patient sent for me in the middle of the night, saying that something had happened. She was right. I have never seen such an explosion as had occurred in the skin of the patient's leg. I said, "You have not told me the whole truth," and she then said, "I will tell you something that I have never told anybody before. I am an epileptic; my attacks come on at night, and I have been taking bromids for years." This outburst seemed to me to be due to the combination of bromid and chlorin, and I would like to ask Dr. Wile to explain what he thinks of this episode. To my mind it does not seem to fit in well with his theory.

Dr. Samuel E. Sweitzer, Minneapolis: In looking up the subject of drug eruptions I have been surprised to find recorded three deaths from the use of boric acid. I had previously considered boric acid as a mild and harmless preparation.

In April I saw an unusual procain eruption in a young woman who had been given a caudal anesthetic. The procain eruption came out within a few hours and presented itself as an acute eruption, which extended around the body in the region of the hip. It was, to me, a very unusual manifestation.

Dr. Charles Wallis Edmunds, Department of Pharmacology, Ann Arbor, Mich.: I wish I might add something to this discussion, but I came to learn. I have profited greatly by the papers I have heard, but have been especially interested in the papers on drug eruptions and in knowing that the dermatologists, when it comes down to the fundamental causes, know no more than the pharmacologists, and they know very little.

Regarding the question of iodids and bromids: It has been known for a long time that there is a marked difference in the time of elimination. Iodid requires about forty-eight hours and bromid much longer. I think Fishman, in 1907, took 15 grain (0.97 gm.) doses of bromid, and found bromid in the urine fifty to fifty-five days afterward. This is very interesting when considered in relation to the chemical reactions of the two drugs. The fact is that the iodid is a foreign substance in the body, and the urine quickly gets rid of it, but as a matter of fact the kidney cannot differentiate between the bromid and chlorid ions. We are taking chlorid all the time, and it is therefore impossible to trace any definite dosage, but probably it is retained in the body just as the bromid is retained. The iodid is a foreign ion and we can trace it, but we cannot do this with the bromid. The kidney tubules apparently cannot differentiate between the bromid and the chlorid, and the bromid keeps circulating in the body for five or six weeks, which explains the difference in the rate of elimination of the two substances.

I was much interested in hearing of the giving of large doses of iodids intravenously. I think we are becoming more prone to give intravenous injections, and yet I wonder whether it is justified. For instance, the iodids and bromids taken by the stomach are absorbed in a few minutes, and large amounts will be absorbed within a very short time, making intravenous medication largely unnecessary. Sometimes the results from the administration of some drugs intravenously are rather unfortunate, and it is well to go a little more slowly. Some firms are putting out large numbers of drugs that can be given intravenously, but I think that pharmacologists are opposed to the administration of most of these drugs intravenously, thus subjecting the patient to a risk that attends the injection of these drugs directly into the blood stream, unless of course there is some definite indication for an extremely rapid administration of the drug.

Dr. Harry E. Alderson, San Francisco: I have a patient whose condition calls for the administration of iodids in the largest possible dosage, and yet she cannot take over 5 grains (0.32 gm.) at a time without having distressing symptoms. She develops a rapid heart, and she has coryza and all the other manifestations of iodism, without having acne. She also has symptoms of hyperthyroidism. At one time she was able to take as much as 30 grains (1.95 gm.) daily for a short period. Once when she had taken none at all for a month she insisted that the coppery taste persisted. As she is a very intelligent woman, I think her statement is worthy of consideration. I should like to ask what can be done with a patient showing this idiosyncrasy or hypersensitiveness.

Dr. Fred Wise, New York: One of the points which Dr. Goldenberg brought up in his very interesting discussion was the use of phenol-

sulphonephthalein and the possibility of that drug producing an eruption. There is no question but that thousands of kidney tests are being made every day, and since we have not heard that any of these patients have had a rash, it seems obvious that there must be a vast difference in the chemical combination in the blood which results from the ingestion of phenolsulphonephthalein and phenolphthalein. I have too little knowledge of chemistry to say what the difference may be, but I think, in view of the fact that we do not get reports of eruptions following phenolsulphonephthalein, that it does not cause the eruption provoked by the phenolphthalein.

The well-known fact that iodids and bromids may provoke deep-seated subcutaneous nodules, bears out Dr. Wile's statement that the ordinary cutaneous bacteria do not play a leading rôle in the causation of iododermas and bromodermas.

In regard to Dr. Schamberg's saying that we should look for leukocytosis in skin eruptions, we have no experience except in bromid eruptions in which the leukocyte count was normal. Whether this holds good in phenobarbital eruptions, I do not know.

Among the points not touched on was the remarkable disappearance of antipyrin and phenolphthalein lesions in spite of the fact that the patient continues the use of the drug. That is a puzzle, and I do not know that any one has said anything that would explain this in any way. Stelwagon and some of the foreign writers say that the eruption will disappear while the patient is taking antipyrin, and may vanish permanently.

Another fact is that a patient may have a bromid eruption, and on stopping the bromids the eruption will persist for a year or longer. I have seen a case like this in a baby who had a bromid eruption from suckling the mother, and the eruption persisted for a year after the mother stopped taking the drug.

I would like to stress the point Dr. Pollitzer made, and that is the question of idiosyncrasy, which, of course, we can talk of in only a vague way. There are some drugs in which idiosyncrasy must play a much more important rôle than in others. Nearly every one may have an iodid eruption if he takes enough of the drug; people have arsphenamin eruptions.

I should like to have Dr. Wile make clear the point as to whether his patient with pemphigus received potassium iodid or bromid.

Dr. Udo J. Wile, Ann Arbor, Mich. (closing): Dr. Goldenberg's discussion brings out a therapeutic suggestion of great value which we have had occasion to employ, and which is very instructive. He said he has been accustomed to give patients with a bromid rash sodium chlorid. The bromid dermatitis can be made to disappear quickly by the intravenous injection of physiologic sodium chlorid solution, which I am sure Dr. Edmonds would not disapprove. In one patient, a man, the bromid reaction was very severe, accompanied by stupor, pallor and palpitation; he was promptly relieved of the stupor and other symptoms after the administration of 100 c.c. of physiologic sodium chlorid solution. In another case the eruption disappeared very quickly after the intravenous injection of physiologic sodium chlorid solution.

I well remember the experiment of Bruch, which Dr. Cole alluded to, and it was one of the best examples of true allergy in the literature. Bruch was attempting to demonstrate iododerma on the basis of anaphylaxis. The patient he had as a control was in the hospital for gonorrhea and, according to his statement, had never taken any iodid of potassium. This blood was taken as a control, together with the serum of the guinea-pig and that of a patient who

had iododerma; following this injection the guinea-pig immediately died with anaphylactic shock. Bruch then gave the patient a few doses of potassium iodid, and he immediately broke out with an intense eruption. Bruch concluded that this man had a hereditary sensitization to iodids. This has never been substantiated.

Dr. Pollitzer's remarks regarding the type of dermatitis following intravenous administrations and that following ingestion are very interesting. I believe the two processes are distinctly different. That the effect when the drug passes through the digestive canal and when it passes through the blood is very different must be self evident. There is a great difference in the results after intravenous injection and after administration of the drugs by mouth.

I do not think Dr. White's case is difficult to explain if one accepts the fact that trauma is a local predisposing feature in drug exanthems. I think we have demonstrated this in the production of exanthems. I do not think it has anything to do with the replacement of the bromid in the blood with chlorin. I think the explanation in this case is based on the element of trauma.

Dr. Sweitzer's remarks regarding boric acid were interesting. I saw a patient this year who developed a marked erythematous rash each time he came in contact with the biborate solution with which his bladder was irrigated.

I wish to take issue with Dr. Wise's statement that any patient taking iodid of potassium will sooner or later develop an eruption. That is not so, and I am sure a large group can take amounts of this drug over many months without developing rash. Those who develop a rash do so after taking a few grains in some instances. This is perfectly manifest in the cases of nursing children who develop a nodular bromoderma from the breast milk of the mother who is taking a few grains of bromid. I believe our experiments have conclusively proved that there is no relation between the size of the dose, and the appearance of a rash in a given case.

INDUSTRIAL DERMATITIS AT THE MASSACHUSETTS GENERAL HOSPITAL*

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The papers of Fordyce,[1] Hazen,[2] Knowles,[3] White[4] and Pusey[5] have already pointed out the many occupations in which an irritation of the skin may be produced. They have described the types of eruption appearing as a result of employment in these various occupations, and have discussed the etiologic factors which have caused these irritated conditions. Of particular value is the paper of Knowles, based on the study of more than 7,000 cases of eczema, which was presented in this city just ten years ago this month. A study of his paper, and of the other papers as well, emphasizes the importance of external causes in the etiology of these pathologic skin conditions. These authors have made a distinct contribution to our knowledge of such dermatoses, and rendered a real service to dermatology and to the afflicted patients.

But have we profited by this knowledge which they have given us? Have not their lessons been relegated to the background in the mass of dermatologic literature of the last few years? For instance, are we not likely to forget the frequency with which occupational cases are appearing in our clinics? Fordyce has stated that 2 per cent. of the total number of new cases at his skin clinic for 1911 constituted occupational dermatoses, and Knowles in 1913 and 1917 estimated that one sixth of all eczema was due to occupation. There is no doubt that at least the same percentage of our skin cases today will be found by careful study to be due to occupational factors.

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* Read before the Section on Dermatology and Syphilology at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

* From the Dermatological Clinic, Massachusetts General Hospital.

1. Fordyce, J. A.: Occupational Diseases of the Skin, M. Rec. **81**:207 (Feb. 3) 1912; Occupational Skin Diseases, J. A. M. A. **59**:2043 (Dec. 7) 1912.

2. Hazen, H. H.: Industrial Skin Diseases, J. Cutan. Dis. **32**:487 (July) 1914.

3. Knowles, F. K.: The External Origin of Eczema, Particularly the Occupational Eczemas, as Based on a Study of 4,142 Cases, J. Cutan. Dis. **31**:11 (Jan.) 1913; Eczema of External Origin, and Its Relationship to Dermatitis, J. A. M. A. **68**:79 (Jan. 13) 1917.

4. White, C. J.: Certain Occupations as Contributing Factors to Diseases of the Skin, Boston M. & S. J. **175**:35 (July 13) 1916.

5. Pusey, W. A.: Industrial Dermatoses, Their Sources, Types and Control, J. Indust. Hyg. **1**:385 (Dec.) 1919.

In this paper it is my purpose to act as the social service worker, that is, to attempt to do a little "follow-up work," and help "carry on" in this broad field in which these pioneers have shown the way. I shall discuss the occupational cases appearing at the Massachusetts General Hospital in the last few years, and emphasize the opportunity presented to us, as dermatologists, to contribute a still greater share to the work of preventive medicine.

FREQUENCY

In making this study of the cases of occupational dermatitis, it was found that no attempt had been made to group these cases in the diagnosis catalogue. Experience in the clinic had shown that the majority were given a diagnosis of dermatitis, dermatitis venenata or eczema. It has been necessary, therefore, to examine all records with the foregoing diagnoses in order to find the cases associated with the patient's occupation. For the three years 1919, 1920 and 1921, there were 921 cases of dermatitis or dermatitis venenata treated in the outpatient skin

NUMBER OF CASES AND NUMBER OF ADMISSIONS

	1919	1920	1921	Totals
Admissions to skin department.....	2,263	2,301	2,580	7,144
Cases of dermatitis	249	365	307	921
Cases of occupational dermatitis	22	47	37	106
Cases of eczema	....	522	564	1,086
Cases of occupational eczema	....	25	23	48
Total cases of dermatitis and eczema....	249	887	871	2,007
Total occupational cases.....	22	72	60	154

department. A critical examination of these records revealed 106 cases in which the occupation was a probable etiologic factor. In more of these cases the relation was not as clear cut and the evidence did not warrant including them in this group. In other words, there were 11.5 per cent. of the cases of dermatitis or dermatitis venenata which were probably industrial in origin.

In a similar manner, the 1,086 cases of eczema for the years 1920 and 1921 were examined. In this group there were forty-eight cases in which there was definite evidence on the record to show that the skin condition was probably derived from the patient's trade or occupation. There were, then, 4.4 per cent. of the cases of eczema from industrial causes.

The accompanying table shows the number of cases occurring in each year and the number of patients admitted to the skin department for each year.

For the year 1921 there were sixty occupational cases among 2,580 admissions to the skin department, so that the ratio of industrial cases

to total admissions, so far as it is possible to ascertain, was 2.3 per cent. The ratio in 1920 was 3.1 per cent. The cases of eczema in 1919 have not been studied, but it is hoped to make still further investigation on this subject.

In the two years 1920 and 1921 there were 132 cases which were caused by occupational conditions. This is 7.1 per cent. of all cases of dermatitis, dermatitis venenata and eczema, or 2.7 per cent. of the total admissions to the skin department.

From a study of these records I feel that the actual percentage is larger than these figures show because of the number of cases, especially of eczema, in which the occupational factor was not mentioned. Furthermore, burns, infected conditions, keloids, etc., have not been examined from this point of view. I believe that it would be a conservative estimate to say that 4 or 5 + per cent. of the admissions to the skin clinic may be caused by occupational factors.

TYPES OF WORKERS

Examination of these 154 cases more closely shows that there were ninety-four, or 61 per cent., male, and sixty, or 39 per cent., female workers, all of them white. The ages varied from 16 to 82 years. There were thirty-one different occupations represented. Housework and allied work contributed forty-seven, the greatest number, to the group. Various washing powders, naphtha soap, soapine and brass polish are the agents most frequently mentioned as the exciting causes. Seven men are included in this group, their occupations providing opportunity for contact with washing powders and cleansing agents. The shoe workers, fourteen in all, formed the next largest class. There were twelve who handled dyes in some form or other. Paints, including furniture polish and varnish and various removers, accounted for ten. There were seven rubber workers, and seven who worked in candy factories, four of the latter among chocolate workers. There were six nurses in the group, and three men in whom cyanid was a probable factor. Among the others, the following types of workers were represented: machinist, photographer, silver polisher, packers (using hay, straw, etc.), baker, tanner, cement worker, nickel plater, tobacco worker, longshoreman, bleacher, upholsterer, waitress, gardener, necropsy room attendant, miller, acetylene worker, labeler, lumberman, farmer, wool worker and printer. A more detailed investigation of these cases is being undertaken, and a further report will be made in a later paper.

THE INDUSTRIAL CLINIC

The investigation of these cases has been greatly facilitated by the Industrial Clinic at the Massachusetts General Hospital. This is a separate clinic through which pass all cases of disease associated with

industrial conditions, or any condition suspected of being associated with an industry. This clinic is one of the first, if not the first, industrial clinic established in a general hospital. The clinic has a very close association with the department of industrial hygiene in the Harvard School of Public Health, and, on the other hand, with the state department of labor and industries. It therefore offers an opportunity for the scientific study of occupational diseases, and also an opportunity for an accurate investigation of the conditions under which the disease or condition may have been acquired. It is possible, then, for a patient with an industrial skin condition, or one suspected of being such, to be referred to this clinic for investigation. This clinic will interview the patient, and report the case to the state department of labor and industries, which will send out an inspector to investigate the particular plant and the particular part of the work which this patient does. Furthermore, this clinic is in position to follow up the patient to make sure that he returns to the skin clinic at proper intervals for treatment; to attend to various details in connection with compensation, if time is lost, and to maintain close cooperation with the various industrial physicians in the vicinity.

PROPER METHOD OF DEALING WITH THESE DERMATOSES

The study of these cases has brought home to me very forcibly several facts which seem essential in the proper dealing with these dermatoses. In the first place, there is the wide variety of occupations in which a dermatitis may arise. The list which I have given discloses some of the types of work, but there are many others to which our attention has already been called. In the second place, there should be a more careful study of the patient. These occupational cases are likely to be lost in the rush of the clinic. They are likely to be considered as an ordinary type of skin disease, for they do not usually present unusual and therefore interesting manifestations. Some present the picture of an acute dermatitis of short duration. Others simulate an eczema of long standing. Others appear as burns, boils, etc., or as other common conditions. We are likely to write a few words of description on the record. We make a diagnosis of acute dermatitis, dermatitis venenata or eczema, or the like, and we prescribe some simple remedy for the relief of the present condition. Often, in the crush of the clinic, little thought is given to possible occupational factors, and still less attention is paid, I am afraid, if the patient is unable to understand or speak good English. The patient is dismissed to make way for the next one without an attempt to study the case or the working conditions. Let me use, as an example, certain cases of eczema in 1920, ninety-nine in all, in which the disease was practically limited to the hands and arms. In fifty-two of these the occupation was given as "housewife" or "at home." There was no indication on the record

that the occupation of any of this group had been considered as a possible cause, and I have not included these among the occupational cases. But I believe that many of them were due to some element in their work. Such cases are lost, not only for the purpose of statistical study, but also for the purpose of investigating the industrial factors involved, and without the knowledge based on the study of such accumulated facts it is a difficult matter to take steps for the prevention of such skin conditions among susceptible persons.

In the third place, there should be a more exact analysis of the job, and a wider knowledge of trade processes and conditions. Pusey has already emphasized the necessity for "more knowledge of the factors which are important in the production of these diseases and in their prevention and control." It is not enough to know that a man is a painter or tanner or dyer or rubber worker. We should find out the active agent in producing his condition, or at least instigate an investigation of his working conditions, of the substances which he handles and of the effect of such factors on the skin. The fact that a man, aged 33, with an eruption on his arms, is a night pumper in a compressed gas factory means little till it is found that at intervals during the night he fills a generator with calcium carbid, wearing only cotton gloves. The same is true of the book packer who is found to handle new books and to have his hands become covered with stains from the covers, or the housewife who is working part of the time in a tobacco factory as a stripper, or the jeweler working with cyanid in the coloring room. The exact knowledge obtained in the study of the processes of vulcanizing and of printing has been of inestimable value in the proper handling of the dermatoses occurring in these occupations. A most valuable feature of the book on this subject by R. Prosser White[6] is the detail with which the trade processes are explained.

PREVENTION

In the fourth place is the fact that the prevention of these dermatoses should receive greater emphasis. There is, of course, the present skin condition to treat; but the real problem is the prevention of its recurrence and the prevention of a similar condition in other susceptible persons. The situation is analogous to the infectious skin conditions. We do not make a diagnosis of scabies or impetigo without taking steps for the prevention of its recurrence and for preventing the infection from appearing in others; but meanwhile we treat the existing condition. The same should be true in the case of the occupational dermatoses—the proper treatment should mean prevention.

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6. White, R. P.: Occupational Affections of the Skin, Ed. 2, New York, Paul B. Hoeber, 1920.

We need, first, to realize the wide variety of substances responsible for these skin conditions; then to make a painstaking inquiry into the individual case, and to make a careful analysis of the work he is doing, and on this foundation attempt to build a rational procedure for his particular kind of work. There has been exact scientific work of this character in the last few years in the study of two occupations, and it seems reasonable to expect that further similar studies will eliminate the skin conditions resulting from other trades. I assume that most readers are familiar with the preventive work which has been done in the case of the vulcanizers and among the pressmen in the printing trade, but the importance of this research work warrants a brief review.

Among the vulcanizers it had been noted that eruptions appeared on the forearms and hands of men using hexamethylenamin as one of the accelerators in the vulcanizing process, especially in hot weather. Working on the theory that under the influence of the acid in the sweat the hexamethylenamin was broken down to formaldehyd, and later oxidized to formic acid, and thus causing an irritation, Shepard and Krall [7] used alkaline solutions for the immersion of the hands and arms of susceptible persons previous to going to work, and found that the condition did not appear.

Among the pressmen there were a number of workers with an eruption on the exposed surfaces. McConnell,[8] after a careful study of the working conditions, inks, cleansing processes, etc., found that by applying a mixture of hydrous wool fat or hydrous wool fat and oil before working, and by using a liquid soap and sawdust for cleansing purposes, the eruption could be prevented.

In both of these occupations the result was obtained by changing the working conditions without changing the man to another job. It is interesting to note that the first report issued by the committee which studied the eruptions among the vulcanizers recommended a change of work; but the later investigations made this unnecessary. This is the usual suggestion made in the treatment of these dermatoses. It is well to remember that there are the two possibilities, in this phrase, one to send the patient to another job, and the other to alter the process or the working conditions in some way. The former is the one usually employed, thus allowing the conditions to remain for the next susceptible person. It is not hard to imagine the difficulty with which a person acquainted with only one kind of work adapts himself to another kind, especially if he has worked at the first one all his life. The most

7. Shepard, N. A., and Krall, S.: Poisons in the Rubber Industry, India Rubber World **61**:75 (Nov. 1) 1919.

8. McConnell, W. J.: Industrial Dermatosis Among Printers, Pub. Health Rep. **36**:979 (May 6) 1921.

rational preventive measure, then, is the one directed toward rendering the working conditions as safe for the susceptible workers as possible.

SUSCEPTIBILITY

The study of these occupational cases emphasizes still further the fact that these persons with eruption caused by their work have undoubtedly become sensitized in some way to a particular substance, or that they are naturally susceptible. At any rate, to be still more indefinite, they are cases of idiosyncrasy or individual susceptibility. The fact so often used in arguing against these cases, that the condition cannot be due to the occupation because the one person affected is the only one in his room, or the only one affected among many who are using the same substances, or working under the same conditions, is no argument at all, of course. It is perfectly possible for only one person out of fifty or a hundred to have an eruption from handling dyes, or to be the only one out of a large gang of machinists who will be affected by oil, etc. I emphasize this fact because only recently before the industrial accident board an employer defended his case by bringing in man after man employed in the same process as the patient and exhibiting them to the board as examples of the fact that the process did not cause any irritation. The case was one of undoubted susceptibility, and yet the board, at last reports, had decided in favor of the employer. Moreover, the same fact is true in these cases that is true in cases of food sensitization, or of suspected food sensitization, because of positive cutaneous reactions; namely, that only a therapeutic test—the matter of omitting a certain food from the diet in one case, and the matter of omitting a certain process or a certain substance in the other case—is the only real test. It is also important to remember in this connection that there are cases of individual susceptibility to extremely minute quantities in the cases of foods and drugs, and that undoubtedly the same fact is true in connection with these occupational cases.

NOMENCLATURE

Finally, the very number of these fairly definite occupational skin conditions suggests the advisability of grouping these cases better for the purpose of statistical and preventive study. Can we not call attention to these dermatoses in a more forceful manner? Would it not help to emphasize them by giving them a more definite place in our official nomenclature? We have the term dermatitis medicamentosa applied to dermatoses from the absorption of medicinal agents. Why can we not adopt some term, such as "dermatitis industrialis" to be applied to this group of pathologic skin conditions resulting from the industry in which the patient is employed? The name "trade eczema"

has the advantage of long usage, but it seems as if the time had come when we ought to cleave these cases of occupational skin conditions from the eczema group and segregate them in a group by themselves. One objection immediately raised is in regard to the multiform character of the lesions caused from various substances. The possible multiformity is apparent; but, as one thinks of dermatitis venenata with its erythematous, papular or vesicular lesions, and of dermatitis medicamentosa with its macular, papular, pustular or verrucous lesions, such objections seem inconsistent. These are examples of a definite etiologic group, but with possible multiform appearance. The importance of this group in the economic and financial life of the employee who suffers such disability, and the loss in efficiency with the consequent financial loss to the employer, serve as an additional argument for the use of a definite name. If some term, such as "dermatitis industrialis," cannot be agreed on, let us at least adhere to the term occupational dermatitis, or agree to group these cases under one or the other of the diagnoses dermatitis venenata or eczema, and use the term occupational as a qualifying phrase, in order that they may be available for proper study.

CONCLUSIONS

1. Seven per cent. of dermatitis venenata and eczema, or almost 3 per cent. of all admissions to a skin clinic in a large hospital, were occupational in origin.

2. It is fair to estimate that 4 or 5 + per cent. of admissions to a skin clinic may be occupational.

3. A more careful study should be made of the individual patient.

4. A more exact study of trade processes should be instigated in case of questionable eruptions on exposed surfaces.

5. The consideration of preventive measures should be a greater factor as we see these cases in the clinic.

6. Some name, such as "dermatitis industrialis," or at least a more accurate place in our nomenclature, should be provided for this definite etiologic group of cases.

421 Marlborough Street.

ABSTRACT OF DISCUSSION

Dr. Richard L. Sutton, Kansas City, Mo.: I wish to thank Dr. Lane for his suggestion of the term, "dermatitis industrialis," for it fits these cases admirably. I also wish to recommend to my fellow dermatologists a splendid little book along this line, "Occupational Affections of the Skin," by R. Prosser White. It is one of the most useful volumes in my library. I found it almost encyclopedic in its scope.

Dr. Joseph Grindon, St. Louis: Attention has been particularly directed during the last several years to the importance of the subject of occupational

diseases, and yet there remains a good deal to be learned in regard to occupational dermatoses. In the first place, what shall we call them? Certainly not "trade eczema." When the causative agent is determined we arbitrarily take the disease out of the "eczema" group and place it in the dermatitis group. The term "trade dermatoses" would be unobjectionable. There are several things to bear in mind in connection with these cases. First, we know only a small part of the subject, and we should all be on the lookout for new forms. Not only in our clinics but in our private practice we often forget to inquire into the occupation of the patient, whereas often the occupation would throw a light on the condition. These conditions sometimes lead to damage suits. There are some cases of malingering. Other cases are exemplified by that of a man with a congenital ichthyosis, which he attributed to his trade. Again, there are cases in which the patient honestly but erroneously believes that an eruption is due to something connected with his occupation. I recently saw a man who took a new job on Saturday. On Sunday he went out picnicking and Monday developed a toxicodendron dermatitis, which he honestly thought was due to his trade. At the same time we must be ready to do the patient full justice and not hastily determine that the condition is unconnected with his occupation when, perhaps, we are insufficiently informed. If we gave a little more thought to a matter spoken of by Dr. Lane, namely, special sensitization, we sometimes would feel that there was more in the contention of the employee. The responsibility of the physician is great. He should make it a matter of conscience and thoroughly consider the question before giving a decision.

Dr. Jeffrey Michael, Houston, Texas: I would like to add to the long list of industrial dermatoses another which occurs in the oil fields, due to crude petroleum. It has no clear-cut clinical features, except that the covered portions of the body are more affected than the uncovered. This is due to the fact, I think, that the clothing is saturated with the irritating oil.

Dr. Moses Scholtz, Los Angeles: This subject interests the dermatologist as he is called on to determine whether the patient is entitled to compensation or not. The hardest thing I find is to tell whether the condition is ordinary eczema and whether it is systemic in origin or occupational. Whether we call it "eczema" or "dermatitis," the conditions are identical conceptions. It is simply a difference in nomenclature. I tried to differentiate morphologically, and my impression is that toxic eczema is likely to be less symmetrical than the occupational variety. Systemic eczemas are likely to affect any portion of the body while the occupational variety is most likely to affect the face, neck or hands. We often see the hands free, and we then have to assume dust or irritation through the air rather than direct contact as a cause. Another point is that the systemic eczemas are more likely to be fluctuating in their course, while those due to external irritation are likely to be more stable. If any one could give us a definite morphologic differentiation of systemic eczemas from those due to external irritants, it would be of great service.

Dr. T. J. Burke, Pittsburgh: I wish to call attention to a preparation in relation to these dermatoses, that known as "Lux." It is much used for washing shirt waists and other garments of that kind. There is nothing on the label or the instructions regarding its use to lead one to think that there is any danger in using it, but I have seen a number of cases in which it had caused a severe dermatitis.

Dr. William Allen Pusey, Chicago: Dr. Lane touched on one point lightly—the necessity of a more intensive study of these occupational derma-

toses. The great difficulty is that the industrial physician or surgeon is interested in other things and is not a trained dermatologist. What is needed, and what I believe is a possibility if it is gone after, is to get some of the foundations, or perhaps the U. S. Public Health Service, to make a real study of this condition. I know that young well trained dermatologists are in great demand, but I still think it is possible to have two or three of the young, well trained men devote their time to this question for two or three years. They could take with them some of the nestors of dermatology. We could be of help as consultants.

Dr. C. H. Ball, Tulsa, Okla.: My impression is that the main thing in a dermatitis is the peculiar idiosyncrasy of the individual. In a large establishment only a few men will have a dermatosis following an irritation of the skin. Possibly one of the worst cases I have ever seen was treated here in St. Louis by a well known dermatologist as dermatitis exfoliativa, and it was due entirely to a well known brand of hair dye.

Dr. S. Ayers, Jr., Los Angeles: I reported six cases of scleroderma with arsenic in the urine. Dr. Sutton had one of these cases. The history in several of the cases was very suggestive of an industrial dermatosis. One of these patients worked in a paper factory and examination of several samples of that paper showed a high content of arsenic. I think this is against the law now, but it is used nevertheless. Another one of the patients, a woman who kept a grocery store, used powdered arsenic in a dish under the counter for killing mice. The duration of her disorder was coincident with the use of the powder.

Dr. Lester Hollander, Pittsburgh: During the last year I treated four severe cases of vesicular dermatitis, affecting the hands and forearms, and in one instance spreading to the face, in workers in the photographic trade. After careful investigation I was able to determine that metol, which is used in the developing of photographs, was the offending agent. The chemical used was manufactured by the same concern in each instance. As I had a great deal of difficulty in clearing up these lesions, I communicated with the Eastman Kodak concern of Rochester, N. Y., regarding the necessity of medical investigation of industrial dermatoses. In this particular instance the industry itself had taken up the problem. Regarding the treatment, two things must be considered, especially when we are speaking of the acute type of trade dermatoses, the treatment of the condition itself and the prevention of its return.

Dr. Lane mentioned the fact that simply removing the patient from his work does not mean that the dermatologic condition is cured. I heartily endorse that view. Regarding the view of some writers that trade dermatoses depend on idiosyncrasy, in the four cases mentioned skin tests were utilized for the determination of the causative agent, but only two of the cases showed an erythema to metol applied in the form of a skin test. This makes one think guardedly how much of a factor idiosyncrasy really is in trade dermatoses.

Dr. A. J. Markley, Denver: It should always be borne in mind that the irritants with which one comes in contact in industrial occupations constitute only one of the factors in the production of these dermatoses. We know that each person has a certain amount of resistance, and when that resistance is broken down by internal conditions, improper diet or focal infection, it requires only a little external irritation to produce a dermatitis. It seems to me wholly unjust that a dermatitis involving the hands and face or considerable parts of the body should be attributed entirely to an external irritation

when that irritation is simply the precipitating factor. It is not just to the patient that he should be dismissed with simply an amelioration of the condition from which he suffers. It is not fair to the patient and certainly not to the employer that the occupation be held wholly responsible for having induced an industrial dermatosis, and it is proper that we investigate the personal conditions of diet and of health of these patients. It has been pointed out that only one of fifty employees may have such a reaction, and it has also been pointed out that removal from his work frequently fails to result in complete amelioration or disappearance of the symptoms. Unless we are prepared to inquire carefully into the entire condition, the internal cause as well as the external, we are not doing justice to the industry, to the patient, to the employer nor to ourselves.

Dr. David Lieberthal, Chicago: I want to stress the point that we should not say "occupational dermatitis" but "dermatoses."

Dr. C. Guy Lane, Boston: I did not talk about the occupations listed, but in my group there were thirty-one. I also wish to emphasize the careful scientific work done by the investigators of these two particular trades, among the vulcanizers and the pressmen. Dr. Sutton spoke of the book of Prosser White. I think it is particularly good in the way in which he explains the trade process. The malingerers have been spoken of and also the fact that all dermatoses appearing in workers are not industrial in origin. That must be taken into account every time. Dr. Pusey has brought up the necessity of studying, and I think we should certainly attempt to clear up these conditions. It was my intention to advocate the use of the the term "occupational dermatoses," in this group, but on talking it over with a member of the hospital nomenclature committee, there was some difficulty about including it among the other Latinized names and the term "dermatitis industrialis" seems very apropos. Someone mentioned the use of skin tests, but my experience with skin tests is that this is not a real test of susceptibility in these cases. The real test is the therapeutic test. Having the man stop his work for a period or changing the process proves the cause of the dermatitis better than any skin test can do.

Note.—The author agrees with the suggestions made in the discussion regarding "dermatosis" and believes that the better term to adopt in classifying this group is "dermatosis industrialis."

PROCAIN DERMATITIS AMONG DENTISTS*

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One has only to turn back the pages of history to be reminded of the enthusiasm with which new inventions and remedies for the treatment of diseases have been hailed. Later, they have either been relegated to oblivion or have found their level in the treatment of a few conditions and often in a few selected cases. The roentgen ray is one of the best exemplifications of this, and the vaccines which were employed for every known ill from eczema to ingrowing toenails are a very close second..

It is equally true that, when an epidemic of disease sweeps the country, possibly becoming pandemic, there is always a certain amount of hysteria associated with it; as, for instance, there have been for the past several years epidemics of influenza; and every one who has a cold, no matter what the type, situation or degree, looks on it as a grip infection. At the present time, dentists have become more or less hysterical over procain or allied products; and if an eruption of any kind occurs on their hands, they promptly put the blame on these pain relieving remedies. The medical journals have published several articles on this subject, and unquestionably some of the cases have been directly referable to the irritation caused by the dribbling on the fingers or lack of care in preparation when giving hypodermic injections of procain and, in one instance at least, solutions containing cocain. But, after analyzing some of these published articles, and making careful investigations in my own cases, I am convinced that there are elements other than the direct action of these drugs to be considered. In speaking of the action of this class of drugs, I shall use the word procain, as that is apparently the most commonly employed, taking for granted that any one of them might have been responsible, unless otherwise noted.

True procain dermatitis is an extremely unfortunate type of disease in the case of the dentist, for it not only is a constant source of irritation and annoyance to him, but it also often deprives patients of a tremendous amount of relief that they cannot otherwise obtain; he is often loath to acknowledge the cause and may continue the use of the drug either from ignorance of its deleterious effects or because he does not want to believe and hopes it will soon get better. I believe that there are few persons so susceptible to the action of procain that it of itself will cause trouble; but it is an acknowledged fact that any one

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working under the physical and mental strain to which men in this profession are subjected is liable to afflictions which would not occur in different surroundings. This disbelief as to the injurious effect of procain, has been substantiated by Dr. Herman Prinz, professor of materia medica and therapeutics in the Thomas W. Evans Museum and Dental Institute, School of Dentistry, University of Pennsylvania, who in a recent communication says:

> We prepare in our Institute the solution as outlined below. We use about 25 or more quarts per year in our various clinics and we have never seen a single case of skin irritation or other disturbances of a local nature arising therefrom. Many dentists keep their syringes and needles immersed in various types of antiseptic solutions, which contain cresol, alcohol, formaldehyd, boric acid, benzoic acid, alkalies of various types and other compounds. When they use the syringe, they remove it with their hands, which possibly means more or less always contamination with these preserving solutions and I assume that some of the so-called anesthetic dermatitis may most likely find an explanation therein, although I do not deny that isolated cases of procain dermatitis may exist. Personally I have used procain since its introduction into dentistry in 1907 in many thousands of cases and I have not seen any single skin reaction therefrom. I have employed it to a very limited extent in powdered form directly upon wound surfaces in the oral cavity and have never seen from it any ill results.
>
> I have had a number of cases of severe skin irritations observed on the fingers of dentists and in all of these cases I was able to trace the origin to the careless use of formaldehyd, which is so freely employed by dental practitioners in the treatment of infected root canals and also for sterilizing purposes.

Dentists have long hours of doing the most minute kind of work over nervous patients, and unless they are particularly phlegmatic, become more or less fagged before the expiration of the day, and in many cases deplorably so before the end of the year. Without this all important factor, the drug which has been of such enormous benefit to mankind might be relatively harmless. The powers of resistance are lower, and the largest organ of the body, the skin, does not have the same general tone that should normally exist. While physicians and surgeons are using these drugs frequently, they are not under the same continuous strain as are dentists; and while there may have been cases of procain poisoning among the former class, I have failed to find any recorded.

Procain is the hydrochloric salt of a synthetically prepared base, para-amino-benzoyldiethylamino-ethanol. Its solution is neutral in reaction. Caustic alkalis and alkaline carbonates precipitate the free base from the aqueous solution in the form of a colorless oil, which soon solidifies. It is incompatible with the alkalis and alkaline carbonates, with picric acid and with the iodids.

The solution is prepared by dissolving 1.5 per cent. of procain in physiologic sodium chlorid solution, by boiling. When this solution, which either should be freshly prepared or should not be older than about a week, is used, 1 drop of epinephrin to from 1 to 2 c.c., 2 drops to from 3 to 5 c.c. and 3 drops to 6 or more c.c. is needed. As stated, this addition of epinephrin is always made as needed. Solutions containing epinephrin must under no conditions be boiled, as that invariably decomposes the epinephrin. For this reason, so-called dental tablets containing epinephrin and epinephrin in combination should not be boiled in the solvent, but should be merely added to the boiled saline or the Ringer solution.

All glassware used in making this solution or in which the solution is kept should be alkaline free glass (so-called Jena or hard glass).

Ready-made solutions containing procain-epinephrin mixtures as obtained from supply houses in bulk, as well as those obtained in ampules, usually decompose within a reasonable time.

There are apparently two distinct types of eruption: (1) the papulovesicular on a markedly erythematous base, usually preceded by pomphlyx-like lesions, accompanied by intense itching, and with little tendency to spread to other parts of the body; (2) a thickened verrucous condition of the ends of the fingers with involvement of the nail bed and hypertrophy of the nail itself. Marked pain is experienced, due to fissuring. It is not unusual for these two types to coexist.

In a few of the following histories there is no doubt that the direct cause was procain, but it is also reasonably certain that it was planted on unusually susceptible tissue. The patients often say that they have been using the same chemical or dye for years without any harm to themselves, and it is difficult to understand why at this particular time they should suffer from its use. It is largely a question of resistance.

When we come to realize what this peculiar change is—what it is that takes place—perhaps on account of overwork, worry, improper eating, eating when tired or exhausted, eating food which is not adapted to the individual patient and, what is worse, not being content with three meals a day, or, probably the worst of all, constipation and its associated gastric symptoms, we will be in a position to treat more intelligently the conditions that arise. One other factor which is quite frequently overlooked is the relationship between the skin and the kidneys, as faulty elimination of the kidneys throws more work on the skin and changes to some degree the character of the sweat.

Lane[1] reports three cases, in each of which there was marked dermatitis following the use of procain—all in dentists of long standing;

1. Lane, C. G.: Novocain Dermatitis in Dentists, Dental Cosmos, 1921, p. 878.

the causative factor in one was particularly clearly defined, for when the patient used rubber gloves, he was entirely free from the eruption, but on the use of procain without the gloves, there was an immediate return. In all his cases, Lane verified his clinical observations by means of cutaneous sensitization tests.

If a clinical diagnosis has been made of procain dermatitis, a positive skin reaction is of the utmost importance, but a negative reaction does not necessarily mean that the clinical diagnosis must be eliminated, for too many factors enter into these cutaneous tests to make them absolutely reliable; but should the second and third tests prove negative, I should be strongly inclined to look for another cause.

Several dentists have told me that they are resorting to the cutaneous test, and others have asked me to do it for them. On finding it negative, they have continued using procain without fear, placing absolute reliance on the sensitiveness of this test. But they must bear in mind that the body resistance may be altered by so many different conditions that they may become susceptible to the irritation of that or any other drug at any time.

REPORT OF CASES

CASE 1.—Dr. H., first seen, April 4, 1921, presented an eruption on the hands which he said had been there for ten weeks, a typical papulovesicular eczema. The skin in several parts was exfoliating; at the joints were numerous fissures, and there was the usual intolerable itching. The patient was nervous and depressed, could not sleep and had frequent attacks of indigestion; in fact, he felt and looked sick. He attributed the eruption to the use of procain. It had been much better for a few days before my seeing him, but became much worse after the use of a new liquid soap. In the course of a few days this same type of eruption had extended to the face and to the feet and ankles. The patient was confined to his bed for several weeks, and on recovery was advised to take a sea trip. On his return, the last of July, the condition was almost entirely well; but, August 19, there was a slight breaking out on the face and fingers, and he told me that he had used procain with gloves but had unconsciously put his gloved hands to his face. From this time on, he steadily improved but was never entirely well. On October 29, there was a marked outbreak on the face, following the use of a medicated shaving soap. Under soothing lotions, this also promptly disappeared. I am willing to agree that at the outbreak of this eruption in February the cause of it was procain, but it might just as well have been any other irritant substance, as was proved by the later eruptions. This patient had been working hard, frequently at night, and was in an excessively nervous condition, with severe indigestion, largely the result of overwork and nervousness. The outbreak following the use of the medicated shaving soap was convincing, to me at least, that the prime cause was any irritating substance, though procain might just as well take the blame for it in the first instance.

As this patient regained his health, the eruption on the hands gradually improved, but there were frequent nerve racking exacerbations of the papulovesicular type, always yielding to treatment, consisting of total abstinence from work and the application of soothing lotions. We searched for every possible

and impossible cause, realizing that it must be somewhere in his house or office. Finally, in discussing the kind of rubber gloves worn, I asked how long he boiled them, only to be told his attendant washed them in tincture of green soap and hung them up to dry. The cause was found and the condition cured.

Case 2.—Dr. R. called me on the telephone, Oct. 10, 1921, saying that he had procain dermatitis. On examination, he had, on several fingers, pomphlyx lesions with occasional vesicles occurring in small groups, mildly inflammatory and accompanied by itching. They presented the characteristic linear formation, which made me feel that they were due to the action of some of the poisonous plants. The patient told me that he had been pulling weeds the previous week, and that while he felt the eruption on one hand was due to procain, he was equally sure it was due to the action of the weeds on the other. Personally, I am inclined to feel that procain played no part in this eruption, which disappeared promptly under mild, soothing remedies and roentgen-ray exposure. As he has since expressed it, his hands are constantly bathed in procain, as his practice is limited to extraction; and there has been no return.

Case 3.—Dr. N. had been in practice only a short time when he came in with a ready-made diagnosis of procain dermatitis. He presented a thickened, fissured condition around the ends of the nails and around the matrix. There was little or no inflammation surrounding it, and no vesiculation. On microscopic examination, this was proved a typical case of ringworm, as unyielding to treatment as they usually are; but on account of the popular feeling regarding procain, this patient always felt he had had a more or less atypical form of that type of dermatitis.

Case 4.—Dr. D. wrote me the following history: He had a severe case of procain dermatitis affecting both hands, particularly the finger nails, which became thickened and hornlike. He was treated several months for this condition before the cause was ascertained, and it disappeared only on discontinuance of the use of local anesthetics. To prove to his own satisfaction that one of this class of drugs was the cause, he conducted the following experiment: Taking Waite's solution, he shook the bottle and rubbed the cork on his arm every day for four days, at the expiration of which time red marks began to appear where he had rubbed in the solution, and the part began to itch. He continued to rub in this solution in the same way for several days; the spots were becoming larger and swelling until there were several blebs which ruptured with the resulting oozing and pus formation. He rubbed in the solution for ten days, and at that time was convinced that the cause of the inflammation on his hands was that which had produced the lesions artificially on his arm. As soon as he stopped these applications the arm began to heal, but the itching remained intense.

Undoubtedly, however, there are many other substances which would have caused his local irritation from friction. I can recall the case of a young boy who had six or eight peculiar looking lesions on his face, which did not seem to fit into any defined category. He was accused of producing them himself by some artificial means and finally confessed that he had been in the habit of pinching up the skin, wetting his finger with saliva and rubbing it vigorously until these spots appeared. In the case of Dr. D., a stronger irritant was used than saliva. After an interval of two weeks, he rubbed in a little more of the solution, with a violent reaction within five hours. He later tried a solution of pure procain, which produced exactly the same result as had

been obtained from Waite's anesthetic. In this case, we have a suspected dermatitis confirmed by sensitization test of the skin carried out to a greater extent than the diagnosis warranted.

CASE 5.—Dr. S. A., aged 25, who consulted me, November 25, presented a severe dermatitis on both hands. On the dorsal aspect, it had been extended nearly half way to the elbow, and not quite so far on the inner surface. It was extremely inflammatory, and more or less covered with crusts and scales, with many points of exudation. There was considerable involvement of the nail bed, with a recession of the matrix and a slight thickening of the nails themselves. To use his own words: "About five weeks ago there appeared on the index finger of my right hand small lesions, like little grains of sand under the skin, gradually developing into red, scaly blotches with a liquid oozing out." Later, there appeared on the finger and thumb of the left hand the verrucous type of eruption, with a thickening around the nail. Three weeks later, the condition extended until there was presented the picture that has been described. Shortly after he noticed the first irritation on the fingers, he was in the woods picking autumn leaves. The severe eruption did not occur until two weeks after that time, but it is not probable that *Rhus* was a factor, especially as there was no history of susceptibility, he having handled the plants on other occasions with impunity. The cutaneous sensitization tests were negative; and, while the patient was absolutely convinced that procain was responsible for the eruption, there has been no recurrence, although he uses the drug freely, but with the greatest caution against its coming in contact with his fingers in any way.

CASE 6.—Dr. F. wrote me that he had been using a solution called Novol for a year, when the fourth finger of the right hand became affected. Thinking it was due to the soap he had been using, he discontinued that, but the condition gradually spread to the other fingers and the interdigital spaces. The eruption was of the same inflammatory character as described in the other cases, accompanied by intense itching, particularly at night. This continued for three months, when his attention was called to the fact that it might be due to the use of Novol and, on the discontinuance of the use of that drug, the lesions healed in about three weeks. This patient also rubbed into his arm a solution of pure procain every day for a week, with the resulting erythematopapular eruption, accompanied by intense itching. Dr. F. is now using Waite's cocain solution and is apparently having no trouble.

CASE 7.—Dr. S. first noticed a thickening around the nail bed of the left hand, with an accompanying inflammation and considerable irritation. A diagnosis of eczema was made by a local physician, and the patient was told to keep his hands out of water—about as sensible a thing to tell a dentist as to urge a neurasthenic inmate of the almshouse to take a trip to Europe. The condition healed promptly under complete abstinence from work, and the application of calamine liniment; but it returned as soon as he resumed practice, and after close questioning it was found that he had been using considerable quantities of formaldehyd. It was difficult to convince him that this was the probable cause as he had such a fear of its being procain dermatitis that he could see no other possibility. However, he discontinued using formaldehyd, is very careful with his injections, and there has been no recurrence in the last six months.

CASE 8.—Dr. K. had been using procain since 1912, with the exception of intervals during the war, when it was impossible to procure it. Later, its use was resumed, and early in October, 1920, the cuticle around the nails began

to harden, and there was severe itching and cracking of the epidermis. At the same time, he also had a severe itching under the ring on the third finger of the left hand. (This, however, is not an unusual occurrence when men wash their hands frequently with soap, which collects under the ring and is very irritating). Within a short time, the inflammation extended over the back of the left hand; and later the right hand was also affected. There was considerable induration with fissuring at times, and superimposed staphylococcic infection. About the middle of November of the same year, he was away for two weeks and the hands greatly improved; but, on his return to the office, the itching and inflammatory symptoms returned, and he received active treatment, besides taking the precaution of always using rubber gloves while administering procain. Six months later, he gave the following report: "At the present time, the epidermis is healing under the finger nails of the left hand, but there is a slight dermatitis where the trouble originally started; and while using rubber gloves and exercising the greatest care, I believe that I am so sensitized that it takes only a minute quantity of procain to start the trouble again."

CASE 9.—Dr. F., for several years, had a dermatitis on the hands during the summer. As soon as the late fall came on, he was entirely free from the eruption, which was practically the same as others herein described; but it returned again with absolute surety in the early summer. This man had his own truck garden and was accustomed to find pleasure and recreation in taking care of it himself. He not only weeded it, but picked his own vegetables. The occurrence of this eruption during a certain season made one suspicious; so he was induced to forego the pleasure of working in his garden the entire summer, and was absolutely free from any type of irritation. Later in the fall, he pulled up the dead tomato plants, and a severe dermatitis resulted within twenty-four hours, convincing him and me that it was a case of tomato plant poisoning and not caused by the use of procain.

In a recent letter from the H. A. Metz Laboratories, they offer no explanation. They are aware of the fact that frequent cases occur, but mention also that as far as they are aware no cases have been reported among surgeons, which they attribute to the fact that the latter class of professional men wear gloves when they operate. They suggest as a remedy that all dentists who are susceptible wear gloves. In this, as in many other dermatologic conditions, it is rarely difficult to effect a cure if complete rest can be secured; but how to prevent a recurrence is the serious question. Total abstinence from the use of the drug is one way; but this is undesirable, as patients are deprived of a wonderful anesthetic and the dentist of a part of his income, for someone else can handle the drug with impunity; the use of rubber gloves is another way, but that also has its disadvantages. I have several times advised the use of the following preparation for leather workers and those in kindred trades who are subject to irritation of the hand on account of certain chemicals, and it has proved of value; and I have suggested its use to several dentists and have had a few good reports: 25 per cent. of hydrous wool fat and 75 per cent. of petrolatum are heated in a water bath; 2 per cent of phenol is added, thoroughly mixed and allowed to cool in a jar. A small quantity of this is rubbed thoroughly

all over the hands before an injection is made, and the excess is wiped off The taste is not especially unpleasant to the patient, though a small quantity of ointment of rose water can replace a part of the petrolatum.

While there is no doubt that procain and the allied products can produce a dermatitis, for any known drug will do this in a susceptible person under certain circumstances, yet I am inclined to agree with Dr. Prinz that the cases are rare, occurring only in those who possess a marked idiosyncrasy, and under particularly unfavorable conditions. It is not so common as is supposed by the dentists themselves, for they catalogue every eruption they may possess as due to that cause; and they are rather difficult to convince to the contrary in spite of their desire to use the drug. I have found few men who adhere strictly to the direction for the preparation and use of the anesthetic, and it may be that these personal deviations play a more or less important rôle in the production of certain dermatoses occurring on the hands.

Spruce and Sixteenth Streets.

INTRAMUSCULAR INJECTION OF TURPENTINE IN THE TREATMENT OF DISEASES OF THE SKIN *

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Subsequent to the publication of Fochier's [1] paper concerning the beneficial effect of the fixation abscess in combating septic disease, many writers, chiefly German, reported good results in a multitude of general infectious conditions. It remained for Klingmüller [2] to introduce the injection of turpentine as a therapeutic agent in the treatment of diseases of the skin. A review of the literature on the subject reveals many enthusiastic reports. We have employed turpentine in the treatment of a large variety of skin conditions during the last year in order to test its therapeutic value.

REVIEW OF THE LITERATURE

Fochier advanced the "fixation abscess" theory in 1891. He believed that virulent septic infections form no pus foci. He sought to produce an artificial abscess by injecting subcutaneously turpentine oil that would "fix," exhaust and beneficially influence the general infection. He employed the fixation abscess in septic and pyemic processes, especially in puerperal fever, with excellent effect. He also believed that the fixation abscess has a great prognostic value, as no abscesses are formed by turpentine injections in severe infections. Among other enthusiastic sponsors of the fixation abscess theory are Senn,[3] Revilliod,[4]

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1. Fochier, A.: Therapeutique des infections pyogenes generalisées, Lyons méd. **67**:555, 1891.

2. Klingmüller: Ueber Behandlung von Entzündungen und Eiterungen durch Terpentineinspritzungen, Deutsch. med. Wchnschr. **43**:1294, 1917.

3. Senn: L'Abscess de fixation, Dissertation, Geneva, 1898.

4. Revilliod, quoted by Senn: Dissertation, Geneva, 1898.

Gauthier,[5] Colladon [6] and Lépine.[7] They employed the artificial abscess with gratifying results in pneumonia, typhus and otitis media. Pic [8] used it with success in severe forms of erysipelas and other streptococcic infections. Sahli [9] and Hodel [10] administered turpentine with good results in influenza and pneumonia.

Klingmüller [11] deserves the credit for utilizing it and attempting to explain its action in a large number of skin diseases. Plato had used trichophytin successfully in 1901 for the treatment of deep tineas. In 1918, Klingmüller sought to find a substance, not containing bacteria or protein, that had the power to produce pus locally and that might be used in deep tineas instead of vaccines. First experimenting with croton oil, 0.01 c.c. in oil solution, he found that it caused severe local reactions. He then tried 0.001 c.c. solutions and found that the deep nodules of inveterate tinea barbae disappeared in a week. There was a local tissue reaction causing the patient considerable pain and some rise in temperature but no ill effect on the kidneys. He then tried croton oil in other pyodermias, such as furunculosis, with success. Pus decreased in the first twenty-four to forty-eight hours. On account of the severe local reactions, he substituted turpentine for croton oil, and he found that purified turpentine in 0.1 c.c. solutions in oil was less irritating. Leukocytosis was noted for two days following the injection. He ultimately found a strength of 20 per cent. of turpentine best suited for his purpose and recorded success in furunculosis, tinea barbae, impetigo and impetiginous eczema; especially gratifying were the results in tinea barbae of the most recalcitrant type after a single injection. Excellent results were also noted in acne, pityriasis rosea and lichen planus. In lupus vulgaris the effects compared favorably with those following tuberculin injections.

Becher [12] made an exhaustive study of turpentine therapy and made the following classification of his findings: 1. Excellent results are obtained in buboes, poorly healing wounds following operations for bubo,

5. Gauthier: Abscess de fixation chez les syphiques indication et modes d'action, Lyons méd. **117**:1021, 1911.

6. Colladon, quoted by Senn: Dissertation, Geneva, 1898.

7. Lépine: Sur une nouvelle methode de traitment de la pneumonie en imminence de suppuration, Semaine méd. **12**:72, 1892.

8. Pic: Abscess de fixation dans l'érysipele, Lyons méd. **117**:109, 1911.

9. Sahli, H.: Ueber die Influenza, Cor.-Bl. f. schweiz. Aerzte **99**:193, 1919.

10. Hodel, H.: Zur Behandlung der Grippen-pneumonie mit Colloidmetallen und Fixationsabscess, Cor.-Bl. f. schweiz. Aerzte, 1919, p. 610.

11. Klingmüller: Ueber die Wirkung von Terpentineinspritzungen auf Eiterungen und Entzündungen, München. med. Wchnschr., 1918, No. 33.

12. Becher: Ueber Terpentinölbehandlung mit besonderer Berücksichtigung ihrer anwendung in der Dermatologie, Dermat. Wchnschr. **71**:957, 1920.

chancroids, eczema, furunculosis, sweat gland abscesses and mastitis. 2. Good results are obtained in prurigo, pruritus, pyodermias, drug eruptions, posterior gonorrheal urethritis, epididymitis and acute prostatitis. 3. Turpentine therapy is helpful when employed in conjunction with other remedies in ulcers of the leg, tineas, especially deep and indurated ones, and in anterior gonorrheal urethritis. 4. Turpentine has no effect in impetigo contagiosa, pyodermias in children and chronic gonorrheal urethritis. In 1919, Fischl [13] reported good results in tinea barbae. Appel [14] reported good results with small doses of turpentine and stated that he did not believe that the muscles have to be avoided in injecting the drug, as first advised by Kingmüller. In his experience the pain was negligible. Sellei,[15] in 1918, used an emulsion of turpentine oil, camphor, anesthesin and liquid petrolatum with gratifying results in acute and chronic eczema, prurigo and universal pruritus. Fever and severe pain were disadvantages. Holzhauser [16] recommended turpentine in tinea barbae, when used in conjunction with trichophytin, and in impetiginous skin conditions.

Müller [17] (1918) favored turpentine in tinea barbae, kerion and pityriasis rosea. In the same year Gravisch endorsed its beneficial effect in tinea barbae and in all skin lesions with inflammatory exudations, such as acute eczema, dermatitis, drug eruptions, erythema multiforme, furunculosis and pyodermia. Other reports indicate good results with the use of the drug in tinea barbae. Pöhlmann [18] (1919) achieved success in the deep type of ringworm and in sycosis vulgaris. Löwenfeld [19] (1919) and Michael [20] (1919) also obtained similar findings in the deep type. Schubert [21] (1919) reported cures in tinea barbae, sycosis vulgaris, furunculosis and swellings of the legs.

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13. Fischl, F.: Ueber Therapie der Trichophytie mit besonderer Berücksichtigung ihrer tiefen Formen, Wien. klin. Wchnschr. **32**:94, 1914.

14. Appel, A.: Zur Technik der Terpentinbehandlung von Hautkrankheiten, Dermat. Wchnschr. **71**:911, 1920.

15. Sellei, I.: Terpentinölinjection bei einigen Hautkrankheiten, Deutsch. med. Wchnschr. **44**:1828, 1918.

16. Holzhauser and Werner: Trichophyia Vakzine mit Terpentin in der Dermatologie, Deutsch. med. Wchnschr. **44**:1253, 1918.

17. Müller, F.: Die Behandlung der Trichophytie superficialis et profunda, München. med. Wchnschr. **65**:697, 1918.

18. Pöhlmann: Diagnose, Verbreitung und Behandlung der Bartflechte, Med. Klin. **15**: 1919, No. 6.

19. Löwenfeld, W.: Zur Frage der specifischen und unspecifischen Therapie der Trichophytie, Wien. klin. Wchnschr. **32**:132, 1919.

20. Michael: Die Behandlung der Bartflechte, Therap. d. Gegenw., 1919, No. 10.

21. Schubert: Erfahrungen mit Terpentininjection bei chirurgichen Enkrankungen, Zentralbl. f. Gynäk. **43**:468, 1919.

Wederhake [22] (1917) approved of its use for streptococcus and staphylococcus infections in surgery. Rüte [23] (1919) recommended it in staphylococci infections such as furunculosis.

Meyer [24] (1918), and Schmidt [25] (1918) reported benefit from turpentine therapy in skin infections and ulcerating chilblains.

INJECTION OF RECTIFIED TURPENTINE IN DISEASES OF THE SKIN

During the last year we have treated, in private, clinic and hospital practice, more than two hundred patients with cutaneous diseases, with turpentine oil administered by deep intramuscular injection. Although a large variety of diseases were treated, those conditions which previously had been reported as benefited by this form of therapy constituted the great majority in our series. The diseases treated were mainly those in which an infectious agent is known to be the cause or in which, as in pityriasis rosea and pemphigus, some form of micro-organism may be the causative factor.

At first a 20 per cent. solution of turpentine in sterile olive oil was employed, but this produced too much pain. A 20 per cent. solution of rectified turpentine was then tried and found to give practically no pain. This also was given up for a solution of 15 per cent. rectified turpentine and 0.5 per cent. each of anesthesin and quinin hydrochlorid in olive oil, which solution corresponds to the proprietary preparation "terpichin." The technic employed for the injection was in all details similar to that followed for the intragluteal injection of insoluble mercury. The dose administered was 0.5 to 1 c.c. every four to seven days for adults, 1 to 2 minims (0.06 to 0.12 c.c.) once weekly for infants and children up to the age of 5, and 4 minims (0.24 c.c.) every four to seven days for older children.

Subsequent to the injection of the terpichin preparation no subjective complaints were reported except for the rare occurrence of pain in the kidney region. At times a trace of albumin was found in the urine. Injections were immediately discontinued when lumbar pain or albuminuria appeared. Following the injection of ordinary turpentine most of our patients complained of excruciating pain and infiltrations at the site of injection and fever. Some were so sick that they were compelled to remain in bed for several days. However, there were

22. Wederhake: Zur Behandlung des Puetpurfiebers mit Terpentin, Zentralbl. f. Gynäk. **41**:843, 1917.

23. Rüte: Zur Frage der Terpentinbehandlung, Dermat. Ztschr. **28**:28, 1919.

24. Meyer, F. M.: Behandlung der Hautkrankheiten mit Terpentinöl, Berl. klin. Wchnschr. **55**:880, 1918.

25. Schmidt, E.: Ueber neuere Behandlungmethoden der Bartflechte, Berl. klin. Wchnschr. **58**:59, 1919.

several patients with severe furuncular and obstinate suppurative follicular lesions, who insisted on continuing treatment because of the almost immediate improvement in their skin condition.

No beneficial effect was observed in exudative nonvesicular dermatoseslike erythema, urticaria or purpura. In one case of severe bullous erythema multiforme, however, which had resisted all recognized methods of treatment, the injection of turpentine was followed by general improvement and the disappearance of the lesions.

Among the vesicular dermatoses no constant good results occurred except partial improvement, as manifested by a disappearance of the pustules in infected eczematoid conditions like eczematoid ringworm, infectious eczematoid dermatitis, impetiginous eczema and varicose eczema. In several varicose ulcers turpentine therapy produced cleaner lesions with a serous discharge and rapid formation of granulation and epidermal tissue. None of the patients with exanthems were treated for fear of causing renal complications. The lesions in three patients with pemphigus were not affected. In one of these the injections were administered in doses of 8 minims (0.5 c.c.) every four days for a period of three months, without effect.

The parakeratotic conditions treated were seborrheic eczema, psoriasis and pityriasis rosea. In the first two no change was noticed. Two cases of pityriasis rosea seem to have been aborted, new lesions did not develop and the old ones faded within ten days after the first injection. This deserves further observation.

No good results were obtained in the hyperkeratoses or in the erythrodermas with scaling. Acne simplex did not yield to turpentine therapy but in acne pustulosa and acne indurata the pustules and deep masses became less marked. It seemed that the turpentine produced improved cell metabolism with absorption of the pus and infiltration.

Although the attempt was made to test turpentine therapy in all dermatologic conditions, we felt that the main indication for its employment was in pyogenic infections of the skin, especially when associated with poor general tone. For this reason most of our cases belong in this group. In impetigo simplex, impetigo contagiosa and perléche the lesions did not disappear as quickly as when treated by local antisepsis. Improvement was the rule in impetigo of Bockhart. Excellent results were obtained in the deeper pyogenic infections accompanied by metabolic disorders and poor resistance. Ecthyma, furunculosis, sycosis vulgaris, lupoid sycosis, abscesses and erysipelas present a group of diseases in which turpentine should be employed as a valuable therapeutic adjunct.

Noteworthy among the cases of sycosis vulgaris were three which had previously resisted all methods of treatment, including roentgen therapy and vaccines, but which responded to turpentine injections as

manifested by a disappearance of the follicular papules and pustules. It is suggested that these injections be employed in conjunction with roentgen therapy in conditions such as follicular infections, when antiseptic or irritating applications are contraindicated. The ravages of lupoid sycosis were stopped in two instances. In recurrent furunculosis cures were obtained by local cleanliness, applications of cool saline dressings, roentgen therapy, a diet low in carbohydrates and turpentine injections. In erysipelas the injection of turpentine was followed by a drop in temperature and local relief.

Lesions of the skin produced by the various fungi responded indifferently. Favus was not affected; tinea capitis of the superficial type did not react; kerion was only slightly affected; but in deep ringworm of the beard some good results were attained.

COMMENT AND DISCUSSION

No positive evidence exists to explain the mode of action of turpentine on the tissues of the body when administered by injection.

Klingmüller advanced the following theories: 1. Turpentine or its oxidation products circulating in the blood and lymph have a purely chemical action rendering the toxins inactive. 2. Turpentine or its oxidation products dispel from the lesion substances which attract the pathogenic fungi. The stronger power of the turpentine then renders the fungi inactive and enables the body to remove them. 3. The similarity between the action of turpentine and specific vaccines can be shown. The organism is stimulated to form substances which are toxic to pathogenic bacteria or have some sort of opsonic action. 4. Turpentine has a marked inflammatory action. If introduced into the circulation, the organism responds with the formation of antibodies and anti-inflammatory bodies. These may combat inflammation and pus formation and weaken or even destroy pathogenic bacteria. If these theories are true, a polyvalent antibody can be produced.

Becher concluded in his review on the opinions of investigators who studied the action of turpentine that there exists a wide difference in opinion. He believed that it is possible to influence favorably specific diseases with nonspecific vaccines and chemicals such as turpentine. He theorized that there may be an activation of the protoplasm or perhaps a group of actions: (1) leukocytosis; (2) irritation to formation of granulation, and (3) antitoxic action.

Rectified turpentine oil, which we employed in more than 90 per cent. of our cases, is formed from ordinary oil of turpentine by redistillation with lime water, in order to remove any acids and resin which may be contained in it. It is a volatile oil containing a large proportion of terpene, with comparatively little oxygen, and possesses a penetrating action. It has been shown that terpenes ($C_{10}H_{16}$) undergo

a partial oxidation in the body and become terpenols ($C_{10}H_{15}OH$). The odor of the original oil or of these derivatives may often be detected in the breath, showing that a small part is excreted by the lungs, and possibly traces may be eliminated by the skin. Some escapes by the kidneys.

It is our belief that just as the elimination of the terpenols or terpenes by way of the lungs and kidneys produces increased bronchial secretions and urinary output, excretion by the skin results in enhanced local cell metabolism. The effect is mainly that of irritation. The blood vessels dilate, a serous exudation with diapedesis of the erythrocytes and migration of the leukocytes follows, and the tissues of the skin are stimulated to new growth. This results in improved nutrition, improved absorption of waste products and tissue repair. The terpene products because of their chemotactic property also aid in phagocytic action against bacteria. It is also known that the terpenes in the body are slightly disinfectant.

The general effects produced by injections of turpentine may be similar to those of counterirritation. The local irritation causes reflex stimulation of the various centers in the medulla oblongata. The vasomotor change leads to an increase in blood supply with consequent leukocytosis, improved absorption and increased removal of toxins. The temperature is lowered. In a case of erysipelas the temperature which had been 106 F. for a week dropped to 102.4 two hours after the first injection of turpentine; four days later the temperature hovering around 102 F. fell to normal after a second injection, and five days later when it was again 102 F. a third injection caused a return to normal, which persisted.

SUMMARY AND CONCLUSIONS

As a result of our experience with injections of turpentine in the treatment of a large number of skin diseases, we recommend its employment in certain conditions. It may be of real value in the pyogenic infections, especially when there is follicular involvement. In such instances the injections may be given in conjunction with the local application of the roentgen rays. Good results were observed in tinea barbae. Further observations should be made for the abortion of pityriasis rosea. In old ulcers the administration of turpentine was followed by evidence of stimulation and a tendency to healing. Fair results were attained in acne indurata. A dose of from 0.5 to 1 c.c. of a 15 per cent. solution of rectified turpentine in sterile olive oil injected intramuscularly causes no pain and gives the best result. The effect is both local and general. Locally there is apparently cell irritation, while the vital centers in the medulla oblongata are reflexly stimulated.

63 West Seventy-Third Street.

A LICHEN PLANUS ERUPTION AFTER ARSPHENAMIN *

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NEW YORK

It is a well recognized fact that the administration of arsphenamin may produce definite dermatoses of which the most familiar type is the erythematous eruption, which in some instances develops into an exfoliative dermatitis.

Recently Queyrat, Louis, and Rabut,[1] Kleeberg,[2] Buschke and Freymann,[3] and Keller,[4] have reported cases of arsphenamin dermatitis with lichenoid lesions. The following case is reported because, following treatment by arsphenamin, the patient developed a condition which in its clinical appearance, in the histology of the lesions, and in the course of the disease was indistinguishable from true lichen planus. While the possibility that this was a mere coincidence cannot be excluded, the evidence to be presented favors the assumption that the eruption was caused by arsphenamin.

REPORT OF CASE

History.—A mulatto woman, aged 40, married, was admitted to the outpatient department of the Presbyterian Hospital, June 1, 1921, complaining of a skin eruption on the right forearm. The history was irrelevant except that her present husband had been under treatment for syphilis. The patient gave no history of primary or secondary syphilitic manifestations. She had suffered for six years from the lesion which was present on admission.

Physical examination revealed a gauntlet shaped eruption confined to the right forearm and hand. It extended from the finger tips to the middle of the forearm, on the extensor and flexor surfaces. The eruption was brownish-red and did not disappear on pressure. The veins shone through. It was slightly scaly except on the palm, which showed a marked hyperkeratosis. The upper limit was serpiginous and extended completely around the forearm. The cervical nodes were palpable, the knee and ankle reflexes were hyperactive. The Wassermann test was four plus. The urine was negative.

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* From the department of medicine of Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital.

1. Queyrat, Louis, and Rabut: Bull. Soc. franç. de dermat. et syph., 1921, No. 2.

2. Kleeberg, L.: Beitrag zur Klinik der Salvarsan Exanthema, Therap. Halbmonatsh. **35**:370, 1921.

3. Buschke, A., and Freymann, W.: Lichen-ruber-ahnliche Salvarsan Exanthema, Med. Klin. **30**:909, 1921.

4. Keller, Philipp: Lichen planus und lichenoide arsendermatitis, Dermat. Wchnschr. **74**:9 (Jan. 7) 1922.

Histology.—A biopsy from the affected area on the right arm revealed slight hyperkeratosis, and atrophy of the rete with a slight prolongation of the rete pegs. There was a slight cellular infiltration into the epidermis. The papillae and upper cutis were infiltrated with mononuclears, plasma and epithelioid cells. The infiltration was rather sharply demarcated in the upper cutis. The connective tissue of the papillae and upper cutis showed an interstitial and parenchymatous edema. The blood and lymph vessels were moderately dilated and surrounded by a sleevelike infiltration of plasma cells. The diagnosis was tertiary syphilid of the right hand and forearm.

Fig. 1.—Leukoderma of right palm: The skin is normal from middle of forearm to palm. This was the only part of the body unaffected by the lichenoid eruption. It was the former site of the tertiary syphilid.

Treatment and Results.—The patient was given arsphenamin and mercuric salicylate at weekly intervals. She received nine intravenous injections of arsphenamin averaging 0.3 gm. each, and six 1 grain injections of mecuric salicylate intramuscularly. During the antisyphilitic treatment the tertiary syphilid cleared up. The skin of the forearm resumed a normal appearance, but the fingers became leukodermic in places. Within three or four hours after the third and each succeeding arsphenamin injection, the patient complained of a burning sensation

in the stomach, and of belching of gas. This indicated arsphenamin intoxication. After the seventh arsphenamin injection, stomatitis, herpes of the lips and vaginitis developed. The mercurial injections were stopped. The ninth and last arsphenamin injection was given, September 1. At this time there were well defined, slightly raised, purplish-red plaques about 1 cm. in diameter, on the left palm and sole. There were a few scattered, lentil-sized, violaceous, ill defined papules on the mesial surfaces of the arms and left axilla.

Second Admission.—As the eruption continued to develop and the patient complained of weakness and malaise, as well as the intense itching, she was admitted to the Presbyterian Hospital, September 8.

Fig. 2.—Lichenoid eruption: The face, neck and chest are practically clear, although a few lesions appear on the face. The right forearm shows the former site of the tertiary syphilid.

Physical examination disclosed slight lacrimation, inflamed nasal mucosa, and exfoliation of the lips. The tongue and buccal mucosa presented irregular raised grayish areas the size of a pea. The heart and lungs showed no evidence of disease; the liver edge was palpable, but in other respects the abdomen was negative. The systolic blood pressure was 120 mm., the diastolic 70. Blood urea, uric acid, and sugar were within normal limits. The blood count was as follows: erythrocytes, 5,100,000; leukocytes, 8,900; polymorphonuclears, 79 per cent.; small mononuclears, 6 per cent.; large mononuclears, 4 per cent.; eosino-

phils, 11 per cent. The hemoglobin was 80 per cent. The blood platelets were normal. The urine showed no albumin, no pus, and no casts. Phenolsulphonephthalein excretion was 40 per cent. in two hours and fifteen minutes.

Two days later the eruption faded, but on September 17 it became more severe. The patient then began to improve rapidly, and was discharged, October 8, with a diagnosis of syphilis and lichen planus.

Third Admission.—She was readmitted to the outpatient service, Nov. 7, 1921, complaining of a generalized eruption consisting of shiny, angular papules

Fig. 3.—Lichenoid eruption. The papules have coalesced in many places, the coffee colored pigmentation is interspersed between many of the papules. The upper back and neck are reasonably clear.

from 3 to 5 mm. in diameter, and from violaceous to deep purple. A few were distinctly umbilicated. These papules were diffusely scattered over the face and neck, the upper portion of the trunk, and the extensor surfaces of the arms. In other areas they became confluent, in some instances forming rings with yellowish-brown centers. Surrounding such patches were areas of yellowish-brown or slate colored pigmentation. The lesions were so numerous on the

flexor surfaces of the arms, the axillae, abdomen, lower back, hips and inner surfaces of the thigh that little normal skin remained. On the extensor surfaces of the upper arms and lower legs there was slight follicular keratosis with pigmentation. The areolae of the nipples were deeply pigmented. The palms and soles showed hyperkeratosis. The nails were thickened and had pigmented longitudinal ridges along their entire length. The lower half of the right hand and arm, which was the site of the former syphilitic lesion, was free from lesions. The eyes lacrimated profusely. The entire mucous membrane of the mouth showed scattered minute grayish-white papules. Similar lesions were found in the vagina. The pruritus, which had been a marked symptom in the hospital, had subsided.

Biopsy.—Section of a lichenoid lesion removed while in the hospital revealed a marked hyperkeratosis with a dipping down of the horny layer into the epidermis, forming dells. There was a marked acanthosis with increased granu-

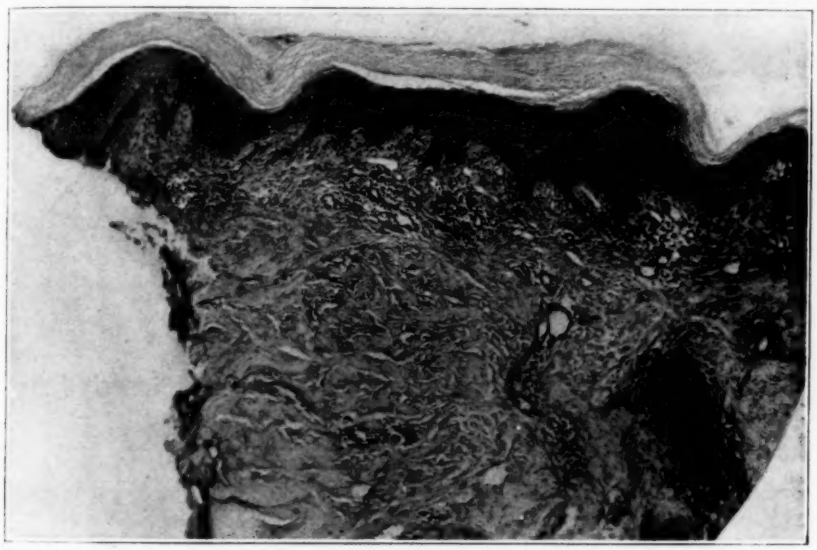

Fig. 4.—Section taken from a papule on the left forearm. Reduced from a photomicrograph × 118.

lar layer, edema, and colloid degeneration of the rete cells. The papillae were widened and edematous. The upper cutis also showed edema, the blood and lymphatic vessels were dilated, and there was a marked cellular infiltration, sharply demarcated from the lower layers.

Under high power the infiltration of the upper cutis and papillae was seen to consist of small mononuclears, larger cells probably of connective tissue origin and melanoblasts, which alone contained pigment granules. The blood and lymphatic vessels of the lower cutis were surrounded by cellular exudate consisting chiefly of mononuclears (Fig. 4).

There was a gradual improvement in her condition, but when last seen, seven months after the first appearance of the lichen planus eruption, she still had a few papules.

COMMENT

There seems little doubt that, had this patient presented the condition just described and given no history of arsphenamin treatment, she would have been regarded as having lichen planus. In view of the fact that the eruption followed treatment, there are three possible interpretations: (1) That it was a mere coincidence. (2) That it was a dermatitis medicamentosa due to arsphenamin. (3) That it was a true lichen planus, in this instance caused by arsphenamin.

Lichen planus, clinically and histologically, is fairly well defined. We have no knowledge of the exact cause, but two hypotheses have been advanced: Pollitzer,[5] Lieberthal,[6] and Hazen[7] believe it is a microbic infection. White,[8] believes that the disease has a neurotic basis. He states that "lichen planus occurs more frequently in educated men and women whose lot in life has been hard." Little,[9] comparing the incidence of lichen planus before and during the war, found a decrease in the latter period, a fact which seems to argue against a neurotic basis. Neither of these hypotheses has any definite proof. Considering the want of knowledge of the cause of lichen planus, this case in which the same syndrome followed arsphenamin intoxication is not without interest.

Previously Reported Cases.—In considering the possibility of arsphenamin causing this eruption, it should be recalled that lichenoid lesions due to arsenicals have been described previously. As far back as 1902, Brooke and Roberts,[10] as well as Barendt,[11] described such lesions occurring in an epidemic of arsenical poisoning from beer. Gans,[12] describing the histology of arsenic melanosis, writes of a case in which the histologic picture was characteristic of lichen planus. This case showed hyperkeratosis, edema of the papillary bodies and a sharply demarcated infiltration of the upper cutis with mononuclears and mast cells. Pigment was scattered through the epidermis, papillae, and upper cutis.

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5. Pollitzer, S.: J. Cutan. Dis. **37**:682 (Oct.) 1919.

6. Lieberthal, D.: J. Cutan. Dis. **37**:682 (Oct.) 1919.

7. Hazen, H. H.: Diseases of Skin, St. Louis, The C. V. Mosby Co., 1915, p. 394.

8. White, C. J.: Lichen Planus, J. Cutan. Dis. **37**:671 (Oct.) 1919.

9. Little, E. G.: Lichen Planus, J. Cutan. Dis. **37**:639 (Oct.) 1919.

10. Brooke, H. G., and Roberts, L.: The Action of Arsenic on the Skin as Observed in the Recent Epidemic of Arsenical Beer Poisoning, Brit. J. Dermat. **13**:120 (April) 1901.

11. Barendt, F.: The Skin Lesions Due to the Presence of Arsenic in Beer, Brit. J. Dermat. **13**:148 (April) 1901.

12. Gans, Oscar: Zur Histologie der Arsenmelanose, Beitr. z. path. Anat. u. z. allg. Path. **60**:22, 1914-1915

Since the widespread use of arsphenamin more typical cases have been reported. Queyrat, Louis and Rabut described an eruption on the tongue resembling lichen planus, clinically and histologically, which occurred after the administration of galyl, a drug similar to arsphenamin. The patient also developed an erythema and pigmentation of the body with intense itching.

Kleeberg also reported a case with an eruption on the dorsum of the hands, and lesions of the buccal mucosa resembling lichen planus following a third course of arsphenamin therapy. Buschke and Freymann reported two cases of acute generalized lichenoid eruption occurring during arsphenamin treatment. Their first case had papules on the chest and flexor surfaces of the extremities resembling lichen planus. The entire skin had a silvery, shiny appearance, felt like a nutmeg grater, and resembled lichen planus verrucosus. Histologically the epithelium was slightly changed. The corium was infiltrated with mononuclears and polymorphonuclears, principally in the perivascular spaces. In the second case, the trunk, flexor and extensor surfaces of the extremities were involved, and the face, neck and chest were free. There was a diffuse grayish-brown to coffee colored pigmentation with a varying degree of intensity. The legs presented follicular keratosis with atrophic centers. The histologic picture revealed normal epithelium, a mononuclear infiltration sharply limited to the upper cutis and brownish-black pigment in the papillae. According to the authors, their first case showed a nonspecific inflammation, while their second case resembled lichen planus histologically, but not clinically. At a little later date Buschke and Freymann,[13] reported a third case which resembled lichen planus somewhat. The eruption was not preceded by a dermatitis but by a slight icterus. Shiny red papules were grouped in rings on the sides of the extremities. Some of these papules occurred along linear scratch marks. There were also macules, follicular papules, and pustules. Biopsy revealed only a slight polymorphonuclear infiltration in the cutis under a somewhat acanthotic epidermis. Hoffman [14] described, as a case of lichen planus, an eruption on the body and buccal mucosa, which appeared after the cessation of antisyphilitic treatment. The patient was given arsphenamin again and the lichen planus eruption became more severe. Sections of a typical papule were characteristic of lichen planus. Keller reported a case which, he said, was lichen planus clinically and histologically. His patient had an eruption confined to the face, body and extremities. There was a diffuse

13. Buschke, A., and Freymann, W.: Weiterer Beitrag zu den Lichenruberähnlichen Exanthemen nach Salvarsan, Dermat. Wchnschr. **73**:945 (Sept. 10) 1921.

14. Hoffman, E.: Arsenkeratose nach hochgradigen universellen Exanthem durch Sulosozylat, Tr. Bonn. Niederrh. Gesellsch., May 9, 1921.

brownish-red pigmentation with a network of split pea sized reddish-brown shiny papules, and there were characteristic lesions of lichen planus on the buccal mucosa opposite the last molar. Smith [15] presented a case before the American Dermatological Association in which an exfoliative dermatitis developed following two courses of arsphenamin. In the discussion of this case it was brought out that some lesions strongly resembled lichen planus. One case of exfoliative arsenical dermatosis with hyperkeratosis reported by Schäfer [16] also presented lesions on the tongue and buccal mucosa which were somewhat like lichen planus. The chief involvement in this case was on the covered parts of the body, which showed a diffuse pigmentation, but in the pigmented areas lichen like papules were also found. Similar cases of arsenical melanosis were studied by Gans and by Habermann.[17]

In all of the cases cited, arsenic was considered undoubtedly the cause of the eruption. In no case was the clinical appearance as close to that of an ordinary lichen planus as in the case reported here. Altogether they form strong evidence for believing that arsenic may produce an eruption simulating this disease. That the eruption described was caused by arsenic was indicated by slight symptoms of arsenic poisoning during a course of treatment, and also by symptoms which are common in arsenic poisoning and are not associated with ordinary lichen planus: conjunctivitis, stomatitis,[18] and palmar keratosis. The pigmentation which was pronounced in this case occurs both in true lichen planus and in frank arsenical dermatitis. In acute generalized lichen planus the papules coalesce and on involuting leave a dark pigmentation which may be confluent. In the case described, however, there was some pigmentation preceding the appearance of papules. This sequence of events has been observed by Jadassohn [19] in true lichen planus.

SUMMARY

1. This case presented the clinical and histologic picture of lichen planus.

2. The eruption followed shortly after the administration of arsphenamin.

3. Cases of arsenical dermatitis closely simulating lichen planus have previously been described.

4. In the case reported, symptoms and lesions of arsenical poisoning support the belief that arsphenamin caused this eruption.

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15. Smith, Morton: Arch. Dermat. & Syph. **4**:554 (June) 1921.

16. Schäfer: Einen Fall von exfoliativer Arsendermatitis und Hyperkeratose, Dermat. Zentralbl. **2**:426, 1921.

17. Habermann, R.: Dermat. Ztschr. **30**:63, 1920.

18. Laurentier, C.: Bull. Soc. franç. de dermat. et syph. **6**:276, 1921.

19. Jadassohn, quoted by Habermann (Footnote 17).

MULTIPLE BENIGN TUMOR-LIKE GROWTHS OF SCHWENINGER AND BUZZI *

S. E. SWEITZER, M.D.

MINNEAPOLIS

Schweninger and Buzzi,[1] in 1891, under the title "Multiple Benign Tumor-Like Growths" described a unique anomaly of the skin.

Crocker [2] gave a very good description of this condition, which we cannot improve on. He wrote: "Clinically, the lesions are soft, round or oval projections, from a lentil to a bean in size, more or less white, with a slight blush or slate color in some of them. Most of them are bladder-like, and can be pressed into the skin by the finger, projecting immediately again like a hernia. The larger ones are flattened and slightly puckered, and harder than the smaller, from which they develop. They undergo spontaneous resolution, and leave only flaccid, loose, foveated scars. They appear very gradually and without sensory symptoms on the trunk, shoulders and thighs and ultimately become numerous, as none disappear entirely, and others keep forming."

Further on, Crocker says: "I have seen very similar lesions associated with fibromata of the ordinary form, when some of them have been absorbed. It is probable that they are the last phase of more than one pathological process."

T. Colcott Fox [3] reported a similar case seen by him, and refers in his article to a case seen by Malcolm Morris and one seen by Van Hoorn. Morris saw the original case of Schweninger and Buzzi and claimed that these three cases were of a similar nature, although no biopsies were made.

Stelwagon,[4] in his book, reported one case which, from his description, seems to belong in this category.

Pusey,[5] in 1917, read a paper on this condition and made a complete report of a case, with microscopic findings. He found a diminution in the elastic fibers.

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* Read at the Forty-Fifth Annual Meeting of the American Dermatological Association, Washington, D. C., May 2-4, 1922.

1. Schweninger and Buzzi: International Atlas of Rare Skin Diseases, 1891, Part 5, Plate 15.

2. Crocker: Diseases of the Skin, Ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 702.

3. T. Colcott Fox: Multiple Benign Tumor-Like New Growths of the Skin, Brit. J. Dermat. **4**:117-119, 1892.

4. Stelwagon: Diseases of the Skin, Ed. 8, Philadelphia, W. B. Saunders Company, 1916, p. 696.

5. Pusey, W. A.: J. Cutan. Dis. **35**:582 (Sept.) 1917.

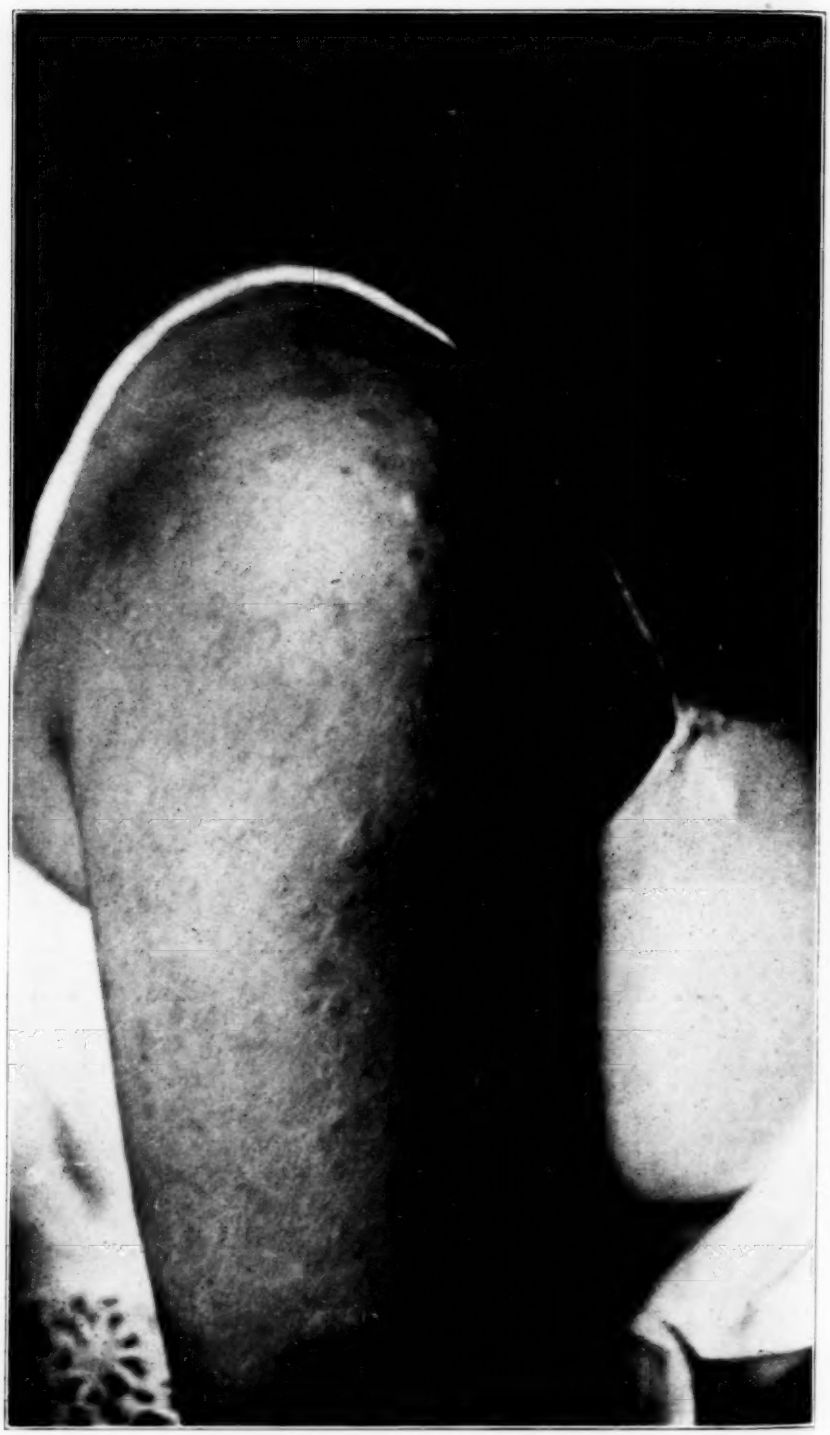

Fig. 1.—Lesions on the right shoulder and arm.

Pringle [6] reported a similar case occurring in a man of 21, showing hard papules, bladder-like tumors and pitted scarring. Pringle maintained that the condition is not a "substansive" disease. A biopsy was not made. Galloway, in discussing Pringle's case, said: "There is no doubt atrophy of the skin, which can be called macular atrophy, but the question is whether this preceding tumor-like appearance of the skin is of the nature of a fibroma, or whether it is some form of degeneration of the white connective tissues, associated with actual atrophy of the elastic tissue, allowing this hernial protrusion, including that of the corium and, to some extent, that of the subcutaneous tissue.

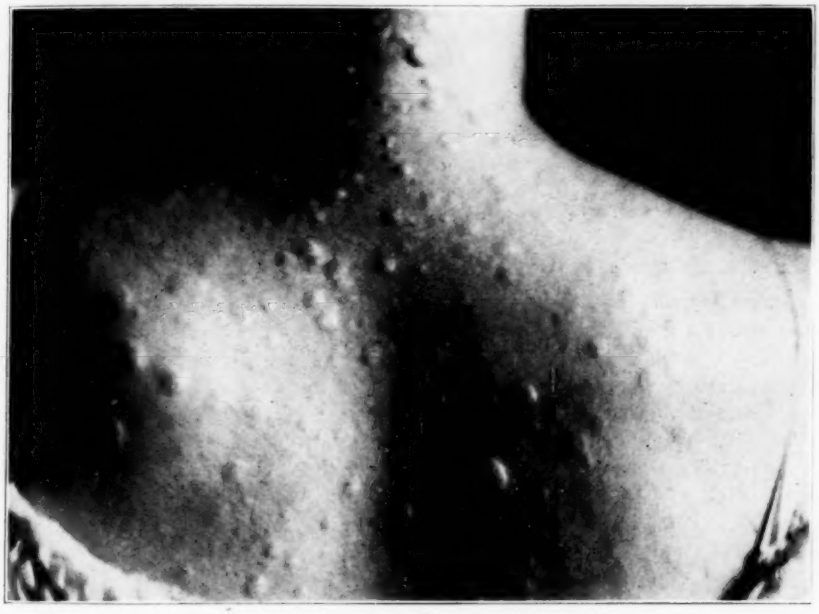

Fig. 2.—Numerous lesions on back.

That it leads on to a condition of atrophy seems perfectly clear, but we agree we have never seen a case of what we call macular atrophy with this excessive amount of tissue, with increase in bulk, so far as the surface is concerned."

Quinn [7] recently presented a somewhat similar case before a meeting of the Chicago Dermatological Society. The discussion brought out the opinion that the lesions were not new growths but a macular atrophy.

Of the nine cases previously reported, all are probably examples of the same condition, except the one mentioned by Crocker, which

6. Pringle: Proc. Roy. Soc. Med. **12**:21, 1919.
7. Quinn: Arch. Dermat. & Syph. **5**:149 (Jan.) 1922.

probably belonged to the fibroma group. Only the original case and the one reported by Pusey have been fully reported.

I am able to report a similar case through the courtesy of Dr. H. E. Michelson. The patient was exhibited before the Minnesota Dermatological Society and was shown to Dr. Ormsby when he visited Minneapolis. The consensus of opinion then was that the case resembled very closely the condition described by Schweninger and Buzzi.

REPORT OF CASE

History.—Mrs. O. C. S., aged 28, a widow, whose family and past history reveal no facts which seem to have any bearing on the dermatologic condition, was a well-nourished and well-developed woman. Her apparent age was no older than her actual age.

The condition present had developed ten years previously, beginning with a single small elevation in the right deltoid region. This elevation was of pea size, hard and bluish-white. It caused her no annoyance, but gradually enlarged to the circumference of a 10-cent piece, and then remained stationary. Insidiously, other similar lesions appeared over the outer surface of the upper arm, the scapular, suprasternal and frontal regions. The patient noticed that the lesions, after being present for some months, retrogressed and became depressed, leaving a wrinkled looking scar.

Examination.—There were numerous small tumor-like projections scattered over the upper anterior and posterior thorax and the arms, and a few on the face and forehead. The lesions varied in size from that of a pea to that of a small cherry. Some were whiter than the normal skin, while others showed a bluish tint, and a few of the lesions had telangiectases over their surfaces. The lesions had the consistency of putty, but there was considerable variation. Some of them were quite soft. The patient stated that the newer lesions were firmer than the older ones. On palpation, many of the lesions could be pushed through a slit-like aperture which admitted the end of the little finger, conveying the impression that the supporting framework had disappeared. The edges of the aperture were smooth and sharply defined. In some locations, the hernia-like lesions had disappeared, leaving the skin over the area thinned and wrinkled in appearance. This scar-like skin was elastic, and when pinched up, seemed to be loosely attached to the underlying tissues. This was evidently the final stage of the disease.

None of the lesions were pedunculated, nor were there any areas of pigmentation or highly pigmented lesions. The surface of all the lesions was smooth, except the wrinkled stage of the older lesions. Sensation was normal, and the location of the lesions seemed in no way to be related to the distribution of the cutaneous nerves. The Wassermann reaction was negative.

Histologic Report.—Three tumors were excised. Two were soft, compressible, old atrophic lesions, while one was an early, firm fibroma-like lesion. The small pieces of tissue excised were hardened in formaldehyd and alcohol in the usual manner, embedded in paraffin and sectioned serially. Hematoxylin-eosin and Weigert's resorcin fuchsin stains were used.

Under hematoxylin-eosin, the epithelium showed marked thinning and complete absence of the rete pegs. There was no hyperkeratosis or parakeratosis;

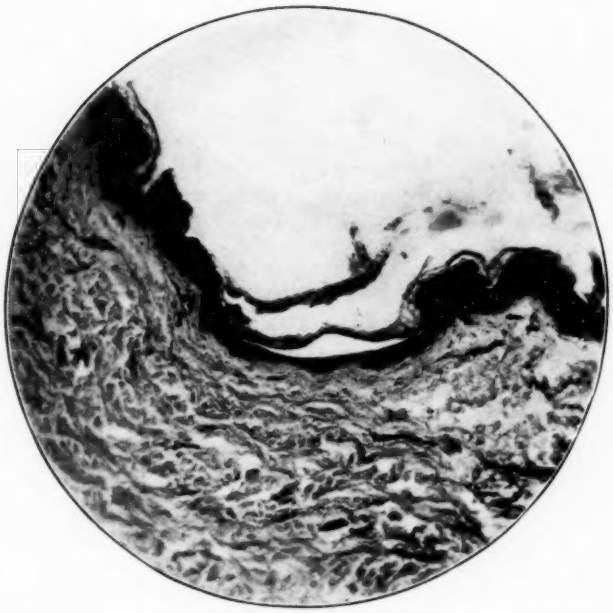

Fig. 3.—Some atrophy of the epidermis and absence of infiltrate in the corium, with hematoxylin-eosin. (Low power.)

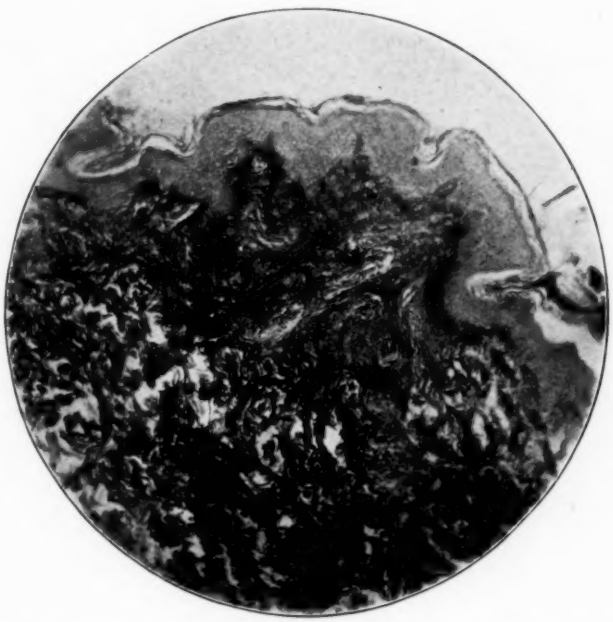

Fig. 4.—New lesion: Elastic fibers present at the periphery of lesion, with Weigert's stain. (Intermediate power.)

nor was there any microscopic evidence of any degenerative processes taking place in the epithelium. There was no infiltration or abscess formation noted in the epithelium.

Examination of the corium revealed: The papillary body projections were lacking. There was no edema, nor destruction of the collagen bundles. Here and there, a few clumps of leukocytes, all of the mononuclear type, were noted. An occasional fibroblast was also seen. There was complete absence of marked infiltration. The sections stained by Weigert's method showed a diminution and atrophy, and in some places complete loss of the elastic fibers, most marked in the upper portion of the center of a clinical lesion. At the periphery of the lesion, the fibers appeared heavier and more numerous.

There were no evidences of new growths. The most marked changes noted were an atrophy of the epidermis and a loss of elastic fibers in the central portion of a clinical lesion.

Fig. 5.—Absence of elastic fibers in upper portion of center of lesion, with Weigert's stain. (Low power.)

These findings correspond to those which have been described as occurring in the tumor-like growths of Schweninger and Buzzi, a condition which this case simulated clinically. This case also corresponded closely to a case reported by Pusey.

In endeavoring to classify the case, one must consider two conditions: (1) fibroma molluscum and (2) macular atrophy. Fibroma molluscum may be looked on as a congenital defect or a nevus syndrome which includes pigmented areas, pedunculated tumors, bone changes, with sometimes kyphosis, and, at times, low mentality. These various conditions are not always present, but typical cases often will show them.

Complete absence of pedunculation, pigmented lesions or pigmented areas is strong evidence against fibroma molluscum in this case. Furthermore, sections from a recent lesion did not show the typical structures of fibroma.

Macular atrophy is considered to be due to a loss of elastic tissue. Bag-like pouching is not usually seen in macular atrophy, but has been noted when some concurrent edematous process caused pressure in the surrounding tissues. From Pusey's studies and from a study of our sections, we are convinced that there is an actual atrophy of the elastic fibers, with a subsequent increase of the fibers about the lesions, forming a perceptible slit-like hernial opening through which the tumor-like lesions protrude. Schweninger and Buzzi did not believe that the lesions were new growths, but remarked that the tumor-like lesions were composed of normal elements.

From a survey of the literature and a study of our case, we are convinced that the so-called tumor-like growths of Schweninger and Buzzi should be grouped with the macular atrophies.

CONCLUSIONS

1. This condition should not be regarded as an entity because histologic study reveals that it is a peculiar type of atrophy and not a new growth.

2. We do not believe that this condition is related to fibroma molluscum.

DISCUSSION

Dr. Jay Frank Schamberg, Philadelphia: This paper has cleared up in my mind the diagnosis in a case of my own presented by one of my associates before the Philadelphia Dermatological Association with a condition unlike any I had seen. We were all very much puzzled as to the diagnosis. The patient, a middle-aged woman, had half a dozen or more lesions on the leg that presented a remarkable aspect. At first sight, one would call them large blebs, and only after we had punctured these very distended baggy prominences did we find that they contained no fluid. A small venule ran through soft, wrinkled overlying skin. On pressing this soft growth, the finger went through a small button-hole like opening, through which you could press down the baggy surface. There were other lesions, which had more or less flattened down, presenting a scarred cigaret paper like wrinkling of the skin, but also with this opening at the base. On account of the resemblance to pemphigus, I suggested that we call it atrophoderma pemphigoides.

I never knew the nature of the disease until Dr. Sweitzer read his paper; but now I am sure from the slit-like opening to which he refers, and the very pronounced atrophy of the skin, that it belongs to this group of cases.

Dr. Walter J. Highman, New York: I was particularly interested in Dr. Sweitzer's presentation because I recall seeing the case Dr. Pusey described at the Cincinnati meeting, and, although I had never heard of the condition before, it struck me that the conclusions of Dr. Sweitzer would be tenable. The condition has all of the attributes of atrophies in general, whether primary

or secondary. Whether we are dealing with scleroderma or the macular atrophies, or with the cicatricial atrophy or pseudopelade, histologically the same elements are present in the skin, in the disturbance of the elastic tissue. Sometimes, there is a complete disappearance of the collagen, and the crumpling back of the elastic tissue in the vicinity of the lesion; and I feel that this button-hole like sensation imparted to the palpating finger must be really due to the retraction of the elastic tissue. There is a certain vagueness of the tissue when the elastica no longer exists. I think it is only a subvariety of the idiopathic atrophies.

Dr. Charles J. White, Boston: We had at the Massachusetts General Hospital a most remarkable case of acrodermatitis atrophicans in which, preceding the atrophy, were the kind of tumors Dr. Sweitzer has described, giving the same baggy sensation. That was as severe a case as I have ever seen, and with this peculiar, progressive symptom which I have seen in but this one instance.

Dr. Francis E. Senear, Chicago: I had the opportunity of studying Dr. Pusey's case with him. The peculiar feature in our case was the fact that all of the tumors were present on the lower half of the face and neck. On the body, we found many of the slit-like lesions that Dr. Sweitzer has described. The patient, who was unusually intelligent, had never noticed any of the baggy lesions preceding the macular slit-like lesions, although we felt that they perhaps developed from the baggy tumor. In the light of Dr. Sweitzer's observations, I think perhaps the patient's observation was faulty and that they were the end-result rather than the preliminary lesions.

Dr. Samuel E. Sweitzer, Minneapolis (closing): This condition struck us as being a peculiar form of atrophy. In regard to acrodermatitis atrophicans, we frequently find a hard nodule in that disease, but this did not resemble that. There are only the small, tumor-like lesions, and the rest of the skin is normal. The patient presented a few lesions on the face, but they were old lesions and had flattened down and did not photograph well.

The condition apparently began with a small nodule, and we purposely cut out a new nodule as well as an old one to see if we could find any evidence of a tumor growth; but we found only a beginning atrophy in that as well as in the older lesion, so, as nearly as we could find out, the condition began with the small tumors, and eventually the atrophy became sufficiently advanced to make some of the tumors flatten out when the patient was lying down, and on standing, they would puff out.

625 Syndicate Building.

THE PRESENT STATUS OF LEPROSY IN THE HAWAIIAN ISLANDS *

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By some, leprosy is supposed to have been introduced into the Hawaiian Islands by the Chinese, many of whom settled there about the middle of the nineteenth century. The reason for this belief rests on the fact that the first name by which the disease as a distinct entity was known in the Islands was *mai pake,* meaning Chinese disease.

Wayson [1] and other leprologists who have lived long on the Islands, as well as others who have recorded earlier observations, do not share this view, but believe that the disease has existed from a more remote period and was probably introduced by sailors or the roving inhabitants of the islands of the South Seas, where from the earliest times it has been endemic. The missionaries who came here in 1820 reported that some of the natives were afflicted with what they called scrofula, "which was not only frequently met with but extremely malignant." [2]

LEPER HOSPITAL AND SETTLEMENT

Soon after the middle of the last century, however, leprosy had made such headway among the native population that in 1865 King Kalakaua called a council to consider means of checking its spread. Segregation of those afflicted and treatment with chaulmoogra oil seemed to offer the most promising means of relief. Accordingly, a hospital for the examination and treatment of persons affected with leprosy was established in November of the same year. It has been in almost continuous existence ever since and is now known as the Kalihi Observation and Detention Hospital. This hospital is situated in the suburbs of Honolulu and consists of a number of small frame buildings pleasantly situated in an inclosure of several acres.

In addition to this hospital, in which it was intended that patients presenting incipient manifestations of the disease and others thought amenable to treatment might be detained, there was established a leper settlement on the island of Molokai, about 80 miles (128 kilometers)

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* Read at the Forty-Fifth Annual Meeting of the American Dermatological Association, Washington, D. C., May 2-4, 1922.

1. Wayson, J. T.: N. Y. Med. Rec., November, 1904.
2. Report of the board of health to the legislative assembly of 1886.

distant from the island of Oahu and Honolulu, the capital of the island group, known as the Kalaupapa Leper Colony. This is situated on a tongue of land 8 square miles (20 square kilometers) in area, projecting into the sea from the north side of the island of Molokai and walled in by the Kalaupapa, a precipitous mountain range or *pali,* 2,000 feet (600 meters) in height, which affords a natural barrier against escape, as well as complete isolation.

The first consignment of patients arrived at this segregation colony in January, 1866. During the first ten years, 1,587 lepers, who should rightly be called patients, were received.

During this decade, the largest number was received in the year 1873, when 487 lepers were consigned to Molokai; while in 1886 there were only forty-three, this being the smallest number received in any single year during this period. An equal variability in the number of patients domiciled at Molokai at different times is also noted. Thus in 1890 there were 1,213; while in 1886, the end of the first decade, there were only 590.

POLICIES IN DEALING WITH THE DISEASE

This irregularity has continued to the present time, on account of variations in policy in dealing with the disease, which governmental changes have engendered, and bears no relation to the actual number of lepers on the Islands, which, in proportion to the number of inhabitants, has of late slightly decreased.

Mouritz,[3] in his treatise on leprosy in the Hawaiian Islands, speaks thus of this phase of the local situation: "The segregation of lepers has been irregular, spasmodic, and efficient only at certain periods. This is only too plainly evident in the testimony supplied by the yearly number of lepers segregated, as per the following figures, which indicate activity and slackness, alternately; depending in the main on election and non-election years." Then follows the yearly consignments from 1866 to 1899, which varied from 43 to 571 (1888). He continues: "The efforts to stamp out leprosy by segregation have taken on the status of a political football, the party in power being assailed by the outs, who return the attack in kind. Both parties have been offenders, using the care and segregation of lepers as a target or a cudgel, depending on the state of the case. The Hawaiians have the majority of votes, and to placate voters and gain their votes the enforcement of the segregation law has been purposely allowed to lapse temporarily." He then makes a plea for federal control, which has since been partially accomplished.

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3. Mouritz, A. A. St. M.: The Path of the Destroyer; a History of Leprosy in the Hawaiian Islands, Honolulu, 1916, pp. 165-166.

This shifting policy in dealing with the problem of leprosy, or rather in looking the problem squarely in the face, is also influenced by commercial and social interests. The unwholesome reputation the Hawaiian Islands received in the death of Father Damien in 1889, and the wide publicity it was given, created in the minds of most people a feeling of dread, even of repugnance whenever the Hawaiian Islands were mentioned. This was not warranted by the facts, and to counteract this wrong impression measures tending to the opposite extreme have been from time to time resorted to. This has resulted in the conflicting reports and the consequent uncertainty that exists in the minds of medical men as to the actual status of the leprosy problem in the Hawaiian Islands.

ESTABLISHMENT OF U. S. CONTROL

Soon after the United States took over the Islands as a territory, the Marine Hospital and Public Health Service was asked to take charge of the leper problem. A cooperative plan was devised in which the department of public health works in connection with the local board of health. But the national control of leprosy has not yet accomplished the desired result, that of taking the most efficient measures for controlling the disease.

An attempt was made with, I am told, an expenditure of about $250,000 for buildings and other equipment, including an ice plant and even microscopes, on the island of Molokai. But here again a change in national policy or procedure took place, and the buildings, which have never been occupied, lie rotting, and the other partial equipment remains corroding and unused. In fact, after a lapse of ten or twelve years no benefit has ever accrued from this somewhat ambitious though abortive attempt to study the subject of leprosy and to employ the most efficient means of controlling this widespread disease, which by some is regarded not only as a local, but also as a national, menace.

TREATMENT BY CHAULMOOGRA OIL

The announcement in 1904 that Power [4] and his collaborators in the Welfare Research Laboratory had succeeded in separating certain fatty acids from chaulmoogra oil led many too enthusiastic leprologists to affirm that if the actual cure of leprosy had not been attained its ultimate eradication from the face of the globe was in sight.

Taub further elaborated the separation of the ethyl esters from chaulmoogra oil, and after their extensive use, particularly in Turkey and Egypt, in the treatment of leprosy, the process was patented in the

4. Power and Gornall: J. Am. Chem. Soc. **85**:838, 851, 1904. Power and Barrowcliff: ibid. **87**:884, 1905. Barrowcliff and Power: ibid. **91**:557, 1907.

United States in 1910, under the trade name antileprol.[5] In these letters patent, full and explicit directions are given for the elaboration of the ethyl esters from chaulmoogra oil as used today in the Kalihi Hospital and Station, as well as at the colony of Kalaupapa on the island of Molokai. The ethyl esters in the form of antileprol were previously used in the Kalihi Hospital at Honolulu by Wayson, between 1910 and 1914,[6] with about the same results as Rogers in India and others were obtaining.

Heretofore, chaulmoogra oil and its derivatives had been given by the mouth. It was disagreeable to the taste and often its use had to be abandoned on account of the deleterious effect on the patient. In 1914, Heiser[7] advocated the use of chaulmoogra oil diluted with an equal quantity of camphorated oil, with 4 gm. of resorcin to every 120 c.c. of the mixture. This was given intramuscularly with encouraging results.

During the World War, letters patent were apparently not considered any more seriously than were other scraps of paper when public necessity required their infraction; consequently Dean,[8] of the University of Hawaii, in 1919, separated the ethyl esters from the crude chaulmoogra oil, as Taub had previously done, and McDonald,[8] and later Wellman, administered them intramuscularly at the Kalihi Hospital. The enthusiasm with which this treatment was received and entered into seems to have been in inverse ratio to the permanent benefit derived. Improvement undoubtedly took place in many cases, especially in the early or mild forms of the disease.

PAROLE OF PATIENTS

Although more or less painful, the discomfort was confined to the buttocks, and patients were able to receive more of the active elements of the drug than they had previously been able to receive by way of the mouth, and with less disturbance to their general health. Consequently, the enthusiasm was not confined to the hospital staff, but was participated in by the afflicted, who saw in this treatment a brighter prospect of being returned to their homes restored to health. Between July 9, 1919 and March 31, 1921, 140 patients were paroled from the Kalihi Hospital as either cured or no longer a menace to the community at large; thus, a semblance of reality was given to this bright outlook.

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5. U. S. Patent No. 957633, May 10, 1910, Washington, D. C.

6. Report of Hawaiian Board of Health, 1912; also personal communication to the author.

7. Heiser, Public Health Reports **29**:2763, No. 42.

8. McDonald, J. T., and Dean, A. L.: The Treatment of Leprosy, Pub. Health Rep. **35**:1959 (Aug. 20) 1920; The Constituents of Chaulmoogra Oil Effective in Leprosy, J. A. M. A. **76**:1471 (May 28) 1921.

During this period, sixty patients were discharged from the leper settlement at Molokai. Of this large number, sixteen have since been returned to the Kalihi Hospital, six have died while on parole, one is known to have escaped from the Islands, and only two have been released from parole as apparently cured, and these prior to the end of the four year period (in which no symptoms of leprosy have appeared, the patient remaining during this time bacteriologically negative) now thought necessary. This still leaves 115 paroled patients from the Kalihi Hospital unaccounted for, as well as those from Molokai.

Two of these paroled patients deserve more than a passing notice. One was a woman of uncertain repute who, on being paroled, entered one of the houses of prostitution in Honolulu, where, after the most intimate exposure of her patrons, who are said to have included soldiers from all parts of the United States, she was finally apprehended as a leper having the disease in its active stage. She is now under treatment at the Kalihi Detention Hospital.

The second patient, also a woman much in the public eye, was discharged from the Kalihi Hospital as cured during the large exodus of 1919, which accompanied the announcement to the world that leprosy was at last completely amenable to treatment. She was exhibited at public gatherings as an example of a cured case of leprosy, and, I am told by eye witnesses, kissed as one "snatched from the jaws of death." This took place during the meeting in Honolulu of the American Press Association and elicited expressions which I will quote from a recent number of what I had considered a conservative weekly publication. "Miss R. B., an Hawaiian woman, had been a leper and was pronounced cured. . . . Miss B., after long treatment at Kalihi, had been among fifty selected to pass across the dark waters of the channels to Molokai—incurable. At the eleventh hour, however, Dr. ——— saw that she was responding to the Dean treatment.[9] The first to be pronounced cured and safe to resume her place among her fellowmen. She is cured."

Again, from a local editorial [10] published during the Press Association meeting:

HONOLULU'S MOLOKAI

The patient who has had leprosy and has been cured may be shy a finger joint, or the tip of an ear, but before God and man he is as clean and free of the disease as a man who has had a carbuncle lanced and has got over it. Hawaii's conquest of leprosy is the greatest achievement of the many of which this land boasts. We not only ask, we urge you to go to Kalihi Hospital today and see this greatest marvel for yourselves, then pass on the word—*Hawaii has cured its lepers.*"

In this star case of "cured leprosy," which was given as much publicity as was the life work and death of Father Damien, who, by the

9. Names given in original article, Leslie's, July 30, 1921.
10. Pacific Commercial Advertiser, November, 1921.

way, was only one of three priests who have died of leprosy in these islands, the patient was returned to Kalihi Hospital a few months later with the disease under full headway, where I had an opportunity repeatedly to observe the case.

During my stay in the islands, I took occasion to examine a few of the many paroled patients who had either discontinued reporting weekly at the Kalihi Hospital as they are required to do, or had never reported since being released on parole. In one instance, a mother and two children had been paroled. One child, although never having presented any symptoms of leprosy, had been hospitalized with the mother and sister, who were lepers. The mother was now bedridden in her home from active manifestations of the disease, and the affected child also presented macular lesions on the skin, with partial paralysis of one eyelid. One child still remained free from symptoms. Both children were attending school. Neither the mother nor the affected child were reporting at the hospital. Their dwelling was in the center of a large taro plantation which furnishes one of the principal articles of food, poi, of the Islands.

Three other paroled patients who were not reporting at the hospital were following their various vocations, one a flower vendor, one a city employee and one a student. While presenting leprous stigmas, the disease, so far as I could ascertain, was not in an active stage. Whether or not these quiescent or mild forms are a menace to the public health, from our present knowledge of the disease we are unable to say.

SURVEILLANCE OF PERSONS AT LARGE

Koch, during his visit here, it is said, obtained lepra bacilli from the nasal mucosa in some of these apparently inactive cases. Two other persons who were not under surveillance of the board of health came under my observation. One was a teacher in one of the public schools and the other was the elevator boy whom I had the opportunity of repeatedly though somewhat furtively examining throughout my stay. In both, there were visible evidences of implication of the facial and ulnar nerves, with consequent paralysis and atrophy of the levator labii and the adductor pollicis and first dorsal interosseus muscles of the face and hands, respectively.

Granting these were mild or incipient cases of leprosy, with our present lack of exact knowledge as to the mode of transmitting or acquiring the disease, we are unable to say whether or not they are a menace to the public health. Here, it is undoubtedly better to err on the side of safety.

In going through one of the large pineapple canneries in Honolulu, I was impressed with the neatness with which the process was accom-

plished, and to see the sealed cans finally passing through a steam sterilizer. This, with the wearing of rubber gloves by those who handled the fruit, was especially comforting to me later, on hearing that three employees had previously been afflicted with leprosy. Since which time, all employees of this particular cannery are examined by a member of the board of health once a month.

On the other hand, from what I saw, it is my belief that there are fewer persons at large afflicted with leprosy in the Hawaiian Islands than in most other countries I have seen where the disease prevails to the same extent. This is due, I believe, to the efficient services rendered by Dr. F. E. Trotter, president and officer of the board of health; Dr. James T. Wayson, the leprologist, member of the board of health and former health officer, and Dr. H. E. Hasseltine, of the U. S. Public Health Service, medical officer in charge of the Kalihi Hospital. At the present time, as for the last three years, all cases of leprosy occurring on the Islands are sent to the observation and detention hospital at Honolulu, where they are paroled or detained, as seems best. In mild cases, the patients returning to receive their weekly treatment are permitted to live at home. There are detained at the present time 187 patients. They are comfortably housed in small wooden buildings, with additional structures for schools, cooking and eating.

Since about the middle of 1921, the treatment consists of weekly injections of all the ethyl esters of chaulmoogra oil, the attempt to isolate any particular acid having given less promising results. The medicament is prepared at the chemical laboratory of the University of Hawaii from the crude oil, which is imported from India. From 1 to 6 c.c., varying according to the weight and condition of the patient, are injected into the gluteal muscle. During the last few months, the ethyl esters have been given intravenously to a selected number of patients in 1 c.c. doses, twice or thrice weekly. The ethyl esters in capsule are also given by mouth in some cases. Iodin, which was formerly given in the proportion of 2.5 per cent., is now discontinued.

At Kalaupapa, on the island of Molokai, of the sixty patients paroled during the period between 1919 and 1921, there are recorded eleven relapses, and two who died on parole. The fate of the remaining forty-seven is unknown.

The treatment carried out by Dr. W. J. Goodhue, resident physician at this colony, is said to be that followed at the Kalihi Hospital. The treatment here, however, is not compulsory. Since the leper colony occupies but a small part of the Island of Molokai, and is shut off from the rest of the island, there is apparently an effort to lift the onus of leprosy from Molokai. This, with the almost complete isolation of the

colony, has evidently led to the abandonment of Molokai as a haven to which all lepers are sent. No cases of leprosy are admitted to these islands from other parts of the United States.

UNSOLVED PROBLEMS

Since the disease became recognized as a public menace, efforts have been made to ascertain its mode of propagation, the influences which favor such dissemination and the best treatment. Distinguished scientists, among whom may be mentioned Koch and Arning, have studied the disease *in loco,* and still the two major problems, those of dissemination and cure, remain unsolved.

CONCLUSIONS

Leprosy was probably introduced into the Hawaiian Islands from without, some time during the last century. The disease spreads rapidly among the Hawaiians because of their intimate mode of living, together with their *laissez faire* attitude in regard to the disease. With this, complete segregation is difficult of accomplishment.

It is most prevalent during school age. It is most common in the male sex. A specific for leprosy has not yet been fully attained.

If one might be permitted to make a few suggestions on impressions gained from a study extending over only a few weeks they would be:

A more definite plan of procedure should be established. If the changing conditions consequent on our elective form of government are allowed to continue to influence the work, it would seem better that it be assumed by a nonpolitical body, such, for example, as the Rockefeller Foundation could furnish.

If the present system continues, there should be, in addition to Dr. H. E. Hasseltine, the efficient medical officer of the Public Health Service now doing all the work of the Kalihi Hospital, a trained clinician, or at least some one appointed or detailed by the Public Health Service, in place of the more indefinite and heterogenous board of health. Not that there is wanting local ability amply to fill this important position if subjected to a nonpartisan, nonlocalized body.

Then, in addition, there should be sent to this field a research worker of undoubted ability—one of the few who like poets are born and not made—to ascertain, first of all, how the disease is acquired. This, in my opinion, is the first great problem to be solved. Its prevention would then be clear; its treatment is already being elucidated and improved. This position should be untrammeled by local influences, and its incumbent should be given a free hand.

Finally, the ethyl esters of chaulmoogra oil undoubtedly have a beneficial effect on most cases of leprosy; in some, it apparently does

harm by aggravating the disease; while in mild or early cases, it apparently, for a time at least, arrests the progress of the disease.

DISCUSSION

Dr. George Henry Fox, New York: I have been greatly interested in the paper of Dr. Corlett. Some twenty-five or thirty years ago it was my privilege to see and treat a large number of cases of leprosy in New York, all of which were imported cases. I remember using Hoang-nan, a Chinese drug, from which I do not remember obtaining great benefit. I remember giving doses of strychnia without any result, but chaulmoogra oil was, in my opinion, then and now a most valuable remedy. Nearly all of the patients that I treated with large or small doses of chaulmoogra oil improved, some of them rapidly. The cutaneous lesions in some cases disappeared rapidly under large doses of the oil. Many of these patients, whether treated with chaulmoogra oil or not, seemed to improve; and I made up my mind that the change of climate in coming to New York was largely responsible for some of the improvement, and I think so now. But that chaulmoogra oil was of value I proved to my own satisfaction then, and I think now that it is the only remedy of great value in this disease. I trust that the ethyl esters will be found to be an improved form of administration, but their precise value does not appear to have been fully determined.

One fact that impressed me strongly was that perhaps no other drug has so many different effects, so much unevenness of action on digestion, as chaulmoogra oil. Some patients could not take more than a few drops without intense nausea, while others could take from 100 to 200 drops daily, and those were the ones that improved most rapidly. One patient under my care in New York for twenty years or more always improved temporarily under chaulmoogra oil, but relapses occurred; so I cannot recommend chaulmoogra oil as a specific or a sure cure. Its varied effect on the stomach in different cases, I cannot explain.

There is one other point in the therapeutics of leprosy that I would like to mention—the psychic treatment. Many lepers are seized by the health authorities and either sent in a box car back to California or elsewhere, or confined in some shanty with food put through a little window on the end of a stick, while the health officer looks at them with a long face and says, "We will do all we can for you, poor fellow, but you have leprosy." No wonder they get worse. If you and I were treated in such a manner, I think we would rapidly deterioriate in health, and perhaps die, whether we had leprosy or not. My opinion is that many of the patients with leprosy if told that it is not an incurable disease will very likely be relieved in mind and benefited physically, if not entirely cured by this encouragement. I think we can accomplish more this way than by the administration of any drug. As I said, I think the change in climate has much to do with improvement. For a long time I believed that leprosy was not contagious. Perhaps I would not say so now, but I would still claim that a leper in any community is by no means as serious a menace to public health as is a case of mild tuberculosis. I have known of patients with the nodular form living for thirty years before the disease had gone on to a "fatal termination" in spite of what our textbooks used to state; and if these patients were encouraged with the hope of a cure and not scared to death, I think they would all improve, if not recover.

Dr. Harry G. Irvine, Minneapolis: I should like to ask Dr. Corlett whether in his observation in the Islands he saw any children with leprosy. In this

regard I should like to relate an interesting experience of my own. We have seen a number of cases in Minneapolis and several in one family starting with a case contracted in Minnesota, so far as we can tell from the history. This woman died with leprosy—I will not say from leprosy—and about a year ago I had an opportunity to examine a daughter, now married and three other children; one was already dead with leprosy. The daughter is just beginning to have thickening of the eyebrows, some loss of hair and three or four nodules. I also examined her husband and two children. At that time there were no signs of the disease in the children, but a few months later her little girl of 3 or 4 years was brought to me for examination. This child then had a peculiar maculopapular eruption, resembling urticaria pigmentosa. It has appeared and disappeared several times, disappearing within a few weeks, and leaving just a little pigmentation. Three months later I saw the child again, and at that time she had three nodules the size of large peas. These were excised and showed all the typical construction of a leprosy nodule. We have never been able to find any bacilli in the nasal secretion or the nodules, but I thought from these findings that the child should be isolated with the mother, at least as a suspect. Both patients were sent to the leprosarium at Carville, La.

Dr. Harry E. Alderson, San Francisco: Dr. Corlett's paper is interesting, and brings up for discussion a subject that is well worth while. Confirming what Dr. George H. Fox said about the beneficial effect of improved hygiene and tonics, I should like to say also that one of the causes of the recent improvement in the matter of the control of lepers in the Islands is the hope that new methods of therapy hold out to the lepers. They feel that there is some chance for them now, and they do not hide away as they formerly did. I have been in Honolulu several times for prolonged visits since 1905 and have been able to observe steady improvement in conditions. An apparent increase in leprosy is believed to have been due to this better cooperation on the part of the natives. More cases are discovered early. On my second visit there I saw a leper who had been hiding away without food, or at least with very little, until he was finally apprehended. When brought into the Kalihi Receiving Station he was in poor physical condition, and the leprosy was correspondingly bad. Under proper feeding, baths, strychnin and arsenic, the physical improvement was remarkable. Such experiences are not uncommon. Similar observations have been made by Dr. George H. Fox.

The last time I was in the Hawaiian Islands I was told that it was much easier to get lepers to report. Perhaps one of the greatest benefits of the new treatment is in the encouragement it offers.

Dr. Corlett spoke of the rather "intimate" life in the Islands. Possibly you might be interested in a few of the details. One good old custom in entertaining guests is to have the entire company occupy one large bed spread on the floor. Perhaps a dozen or more may be accommodated in that way. It is common for entire families and sometimes more than one family, to occupy the same bed. One of the popular native dishes, "poi," is made by pounding out the tara root in a large bowl. I have seen natives laboriously pounding out this food in the hot sun, perspiring over it, and even sneezing in it. The final product is a pasty, starchy raw mass, and it is delicious.

The Hawaiian climate is warm and even, except in the mountains. It is like one huge incubator. At times the humidity is quite pronounced. Conditions for the growth and spread of all kinds of bacterial, insect and vegetable life generally are ideal. In more temperate climates where hygiene conditions

are better, of course the spread of leprosy is necessarily much retarded. In tropical and subtropical countries all of the conditions favorable for the spread of bacterial diseases are present.

DR. A. W. STILLIANS, Chicago: Chicago has a small colony of lepers, and we have had an opportunity to try the new form of treatment to some extent. From our experience we feel that the ethyl esters have had a much more rapid effect on the cases than either chaulmoogra oil or Sir Leonard Rogers' sodium gynocardate. Our first patient was under treatment for two years and four months before being discharged as clinically well, and is still receiving treatment every week. Our other patients have been sent to Louisiana because our facilities for treatment are not good, in that we cannot allow the patients any freedom in the open air.

DR. THOMAS CASPER GILCHRIST, Baltimore: I am glad to see that they are not worrying the patients so much. If patients with syphilis and tuberculosis were worried as those with leprosy are, we would not see those patients as we do. I remember one patient that came to Johns Hopkins and another that came in from Virginia; the latter was almost dying from starvation. I wonder if in Biblical times all diseases of the skin were not called leprosy. Josephus refers to 60,000 cases of leprosy at one time; those cases could not have been leprosy. They were probably cases of itch. I wonder whether scabies, because of the idea of its being contagious, was handed down as leprosy before Hansen found the bacillus, and whether the public has its idea of the great contagiousness associated with scabies and that that might be the explanation of the idea.

I had a case two years ago, a bad nodular case of the face and body, in which I began to administer chaulmoogra oil in small doses. The patient stood it pretty well, and I thought I would try radium and the Kromayer lamp on the nodules on his face to see whether they would disappear more rapidly, and use the chaulmoogra oil on the other lesions. I was delighted to see how quickly the lesions on the face disappeared. When the patient came in, sections were taken and one of the nodules was curetted; in the smear we found the lepra bacilli. The chaulmoogra oil in that case improved the condition very much. The effect of that and cheering and feeding him was remarkable.

DR. E. L. MCEWEN, Chicago: I wish to refer to two points. The first concerns the relation of newspaper activity to the persecution of lepers. The first leper to remain any length of time in Cook County Hospital was admitted as a patient with tertiary syphilis. A few hours later a correct diagnosis was made, and the man was placed in a room by himself. A turmoil was expected over the situation, but for some reason the matter was scarcely referred to by the newspapers; only one conservative evening sheet carried scare-headlines for one issue. As a result of this newspaper quiet the man stayed in the hospital for six weeks, while his deportation was being arranged, entirely without opposition. Since that time a number of lepers have passed through the hospital without a protest. The second point concerns the beneficial effect of simple tonic and hygienic treatment. The extensive, open lesions of the leper to whom I have referred healed completely with six weeks of good food, rest and tonic medication.

DR. HARVEY P. TOWLE, Boston: I would like to call particular attention to one point brought out by Dr. Corlett, namely, the influence of the universal public fear of the disease on the treatment of the disease and the handling of lepers. As Dr. Gilchrist has said, the public fear of contagion dates back to Bible times and farther and continues today. The effect is reflected in our laws. The leper is legally torn from his family and segregated with his fellow victims

far from men and amid surroundings which, in any other disease would cause an outburst of horror and indignation from the public. As it is now, the public merely sighs with relief when the leper is hurried away—and forgets him. It is our duty to educate the public to more humane treatment. To accomplish this we must seek exact knowledge of how the disease is spread, its incubation period, and other factors. We who treat leprosy know that in this country it is not as contagious as syphilis or tuberculosis. But, unfortunately, we are unable to convince the public. It therefore seems to me that we should methodically and scientifically gather data concerning the propagation and spread of the disease and seek to give them the widest publicity. Once we have induced the public to regard the leper more humanely and to provide for him, at least as well as for the convict, we shall have increased the potency of our therapeutic remedies immeasurably.

Dr. William Thomas Corlett, Cleveland (closing): Little difficulty is usually experienced in finding the bacillus of Hansen in a lepra lesion. A frequent cite of an early invasion is on the ear. If the ear is punctured and a droplet of blood squeezed out and placed on a slide and treated in the usual way for the acid-fast bacilli, numerous groups or clusters are shown if lepra is present. It is more difficult to find them in macular, particularly in the late macular or atrophic, lesions.

In the intravenous administration of the ethyl esters the initial dose at the Kalihi Hospital is 1 c.c., repeated after a few days or according to the reaction. Naturally, all patients do not tolerate well this form of administration.

In some of the instances, notably the one cited by Dr. Morrow, a small blood vessel is entered even when giving the ethyl esters intramuscularly. This, if the quantity is large, is followed by a severe reaction. I am particularly anxious to add a word on the point brought out by Drs Fox, Gilchrist and Towle, namely, the degree of contagiousness of leprosy, and the apparent immunity enjoyed by some who are exposed to the disease. I have on several occasions, in discussing this disease, cited the testimony of the Sister Superior of the leprosarium in Trinidad, who during a period of thirty-five years had not seen a Sister employed as a nurse contract leprosy. I have always interpreted this as an indication that the disease is, under ordinary circumstances, feebly contagious. More recent experience, however, leads me to believe that cleanliness and aloofness are two of the factors which render the nurse more immune to leprosy than others who live more intimately with those afflicted with the disease. Father Damian may be cited as an example. For if the reports of his life while at Molokai be true, he neglected the ordinary precautions of contact and even of cleanliness. I should ascribe about an equal degree of contagiosity to leprosy and tuberculosis; certain factors of environment and racial susceptibility must be recognized in both diseases.

The Hawaiians seem to be particularly prone to leprosy, and to a less extent to tuberculosis—two causes which are acting in the extermination of the native race on these Islands.

Children are especially likely to contract the disease; the records of the Board of Health at Honolulu show that it is largely a disease of school age, and to the intimate life of children at school is attributed the spread of leprosy in Hawaii.

Several members have mentioned the importance of hygiene in the treatment of leprosy, which I believe, next to complete segregation, is one of the important things to bear in mind in controlling the disease.

THE USE OF ULTRAVIOLET LIGHT IN ERYTHEMA INDURATUM *

E. LAWRENCE OLIVER, M.D.

BOSTON

As this paper is based on observations of only five cases of erythema induratum treated with the Kromayer lamp, it seems quite unnecessary to review the literature of the disease or to compare this method of treatment with the results obtained from various other methods of treatment. Neither do I intend to review the literature of the treatment of disease with ultraviolet light in general, for I have found no reports of cases in which the light was used in exactly the same manner in which it was used in this group of cases. General exposure of the body to ultraviolet light, or general exposure of the legs, may prove valuable, but as this paper deals with the effects of the local application of the Kromayer lamp on the individual indurated areas of erythema induratum, the methods are not comparable.

At the outset let me state that I am referring to erythème induré des scrofuleux of Bazin occurring almost exclusively in young women or girls, a disease which I believe should be differentiated from the type occurring in middle-aged women which, according to Whitfield, has nothing to do with tuberculosis, and also from the atypical cases belonging to Darier's sarcoid group.

I believe the five cases here reported all belong in the tuberculous or tuberculid group. All occurred in women under 30. All were in the characteristic situations, the posterior and outer aspects of the lower half of the legs. All of the patients had poor peripheral circulation evidenced by cyanosis or cold feet or both. The one patient with a unilateral case showed evidence of a healed tuberculous gland in the neck, which was, except for its unilateral location, in every respect characteristic of erythema induratum of Bazin.

The treatments were carried out by pressing the quartz glass window of the Kromayer lamp firmly against the indurated areas for from one to two minutes to each area. When the lesions were small the healthy skin outside the area was protected with paper or zinc oxid plaster. The Kromayer lamp was used on a 110 volt direct current and was run at full strength for ten minutes before applying it to the indurated areas.

The following five cases illustrate the probable value of this method in the treatment of erythema induratum of the tuberculous or tuberculid type.

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* Read at the Forty-Fifth Annual Meeting of the American Dermatological Association, Washington, D. C., May 2-4, 1922.

REPORT OF CASES

CASE 1.—A woman, aged 24, single, well developed and well nourished, who worked in a biscuit factory and was on her feet nearly all day, had had indurated areas in the calves of her legs for two years, somewhat better in summer but never clearing up entirely. She complained of cold feet and occasional swelling of the ankles and legs. She was first seen by me on Oct. 5, 1919. She then had two deep seated indurated areas in the right lower calf and three in the left lower calf. There was no history of tuberculosis and no evidence of tuberculosis elsewhere. There were no ulcerations or scars. The Wassermann reaction was negative. The legs were slightly cyanotic, especially over the indurated areas.

At the first visit one area, 1½ inches (3.81 cm.) in diameter was treated with Kromayer lamp with firm pressure for two minutes. On October 13, she reported that the area treated became blistered the day after treatment; it became hot, red and tender, and the ankle swelled so that she stayed in bed for two days. When seen on October 13, eight days after the first treatment, there was a dried crust covering the area treated; the swelling and pain had subsided, and the induration had entirely disappeared. At this visit the other four areas were treated in the same manner, but for only one minute to each area. One month later the induration had entirely disappeared leaving the skin of these areas purplish bronze, but otherwise normal in appearance.

Two years later, November, 1921, the skin of these areas was still discolored, but she had had no return of the indurations.

CASE 2.—A woman, aged 30, single, weighing 120 pounds (54.4 kg.), whose occupation was housework, had always had cold hands and feet. She was first seen on May 8, 1920. The trouble had been present four years, clearing up every summer but "worse than ever this spring." She complained of getting tired easily and of swelling of the legs toward night, with discomfort rather than pain. There was no history or evidence of tuberculosis elsewhere.

Locally she showed two deep-seated areas of induration about 1 inch (2.54 cm.) in diameter on the outer lower calf of each leg. There were also about a dozen small pea-sized indurations in the calves. The Kromayer lamp was used, the window being pressed against each of the four large lesions, one minute to each. Eighteen days later she came to me again. The burns had hardly troubled her at all, while the indurations had almost entirely disappeared. I did not see her again for a year, when she reported that all the lesions disappeared within six weeks after the treatment, and that she had had no recurrence during the next winter. All the areas treated showed brownish pigmentation, but there was no trace of induration.

CASE 3.—A woman, aged 22, single, a stenographer, had always been well except for trouble in the left eye since early childhood, which was diagnosed as tuberculous keratitis at the Massachusetts Eye and Ear Infirmary. Circulation in the hands and feet had always been poor. The present trouble had existed for six years, becoming somewhat better each summer. At her first visit, April 16, 1921, she showed small and large indurated areas on the calves and outer surfaces of the lower part of the legs. None of the lesions projected appreciably, but all were purplish and deeply indurated on palpation.

The Kromayer lamp was applied to one large induration on the right calf for two minutes. Eight days later this lesion showed a drying crust, but the induration had entirely disappeared. She had had a severe reaction to the light and was in bed for two days after the treatment on account of pain and

swelling. On April 24, five more areas were treated for one minute each. On May 7, all areas treated showed complete disappearance of induration. On this date the remaining indurated areas were treated. During the summer the trouble almost entirely disappeared, but the next autumn, on Nov. 21, 1921, she had three new indurated lesions, which were treated in the same manner. On Dec. 21, 1921, she was practically well. There were no palpable lesions, but there was marked pigmentation at the sites of all the old lesions. Since then she had had a few new small indurations which have disappeared, except for pigmentation, after a single treatment with the Kromayer lamp.

CASE 4.—A woman, aged 22, single, a hospital nurse, had always been well except for a tuberculous gland in the neck three years ago. This softened and was opened leaving a scar 2 inches (5 cm.) long on the right side of the neck. She was first seen May 13, 1921. The present trouble began while she was in training one year before. Her general health was excellent.

On the lower portion of the right calf she had two marble-sized deep indurations. The legs were somewhat bluish. On May 13, 1921, one of the areas was treated with the Kromayer lamp, one minute with pressure. Six days later, May 19, 1921, the induration had almost entirely disappeared from the treated lesion, which was covered with a drying crust. On this date the other lesion was treated.

In March, 1922, the patient reported that both lesions had entirely disappeared a month after the last treatment, and that there had been no recurrence.

CASE 5.—A woman, aged 24, married, seen on May 18, 1921, had always been well until the present trouble began, a year before. There was no history or evidence of tuberculosis except tuberculous glands in the neck during childhood. The feet and legs were always cold and bluish. She had received much potassium iodid without benefit. The Wassermann reaction was negative. She had been getting steadily worse during the last six months. She complained of swelling in the legs and ankles toward night.

When examined she had five large deep-seated indurated areas in the calves of the legs. At her first visit, two areas were treated one minute each with pressure. One week later these lesions were covered with drying crusts; the induration had nearly disappeared. The three other lesions were treated for one minute each.

Sept. 15, 1921, she said that she was greatly improved. During the last winter she has been on her feet all day; three new lesions developed which have all responded to treatment, the induration disappearing from each in a week or two after treatment.

CONCLUSION

None of these patients had had ulcerations at any time, so that none of the cases were examples of the severest type of the disease. Furthermore, it is impossible to draw definite conclusions from such a small number of cases. I feel, however, that the uniformity of the results from treatment of the individual lesions in these cases justifies the hope that this method will prove of considerable value in the treatment of this obstinate disease.

DISCUSSION

DR. FRED WISE, New York: The reason I hesitate to discuss the paper is because my experience is limited in the use of the ultraviolet light in this disease. I have had only three cases treated in this way. In the clinic with

which I am connected, we are accustomed to use the roentgen ray in erythema induratum, with excellent results, so the ultraviolet light has rarely been used. The results in three cases have been very good, but not better than the results from roentgenotherapy.

Dr. A. W. Stillians, Chicago: I wish to testify to the value of this method, which was one of the first practical things I learned about ultraviolet light therapy. I think it is a safer method than roentgenotherapy, especially in the hands of those who have not had much experience in roentgenotherapy. According to my experience, it is very easy to cause irritation with the roentgen ray in lesions of the leg.

Dr. E. L. Oliver, Boston (closing): I offer as a suggestion to those who are using the Kromayer lamp in the treatment of this disease that they press the window of the lamp against the lesions for one minute.

Abstracts from Current Literature

THE SUPERFICIAL REACTION OF RADIUM AS A GUIDE TO DOSAGE. William S. Newcomet, Am. J. Roentgenol. **9**:34, 1922.

The thesis of the paper is that radium effects cannot be measured by multiplying the time by the quantity of radium, but that larger quantities produce a relatively greater effect in a less number of milligram hours.

HIGH VOLTAGE X-RAY WORK. W. D. Coolidge and W. K. Kearsley, Am. J. Roentgenol. **9**:77, 1922.

A paper devoted to the apparatus for and technic of very high voltage roentgen-ray currents in therapy.

THE ULTRAVIOLET RAY IN THE TREATMENT OF ROENTGEN-RAY TELANGIECTASIS. H. H. Hazen, Am. J. Roentgenol. **9**:101, 1922.

The active ultraviolet lamp, using a compression lens has been found to cause obliteration of vessels of telangiectasis following the roentgen ray. Two treatments of from fifteen to twenty minutes in each area have been found sufficient.

THE RELATION OF TEMPERATURE CHANGES TO ROENTGEN-RAY SKIN REACTIONS. Charles L. Martin and George T. Caldwell, Am. J. Roentgenol. **9**:152, 1922.

Observations recently published make it seem likely that the temperature of the irradiated skin may be a factor in the production of a reaction. Clinical support for this supposition has been had in the observation of patients who had areas treated in the axillae, in folds of skin in obese patients, beneath pendulous breasts, and over the buttocks on areas likely to come in contact with a chair. Areas which were covered by a belt, or heavy dressings or by ointments, etc., seem to show more intense reactions. Experimental work on rabbits was done in which areas of the abdomen exposed to heavy doses of the ray were partially covered with bands of adhesive plaster. The effect on the skin was that the superficial areas were pulled away with the plaster on removal about ten days later. This seems to justify the warnings issued by some roentgenologists that adhesive plaster should not be applied to irradiated areas. Other experiments seemed to indicate that a covering placed over an exposed area for a number of days after it had been irradiated increases the degree of skin reaction obtained. Attempts at cooling the skin by means of an ice bag for several days after irradiation seem to accentuate the reaction obtained.

Goodman, New York.

GUMMATOUS CERVICAL ADENITIS. W. P. Coues, Boston M. & S. J. **187**:65 (July 13) 1922.

A short review of the literature on this subject is given, detailing especially a case reported by Wile in 1912. An additional case of probable syphilitic infection of the cervical glands is reported.

Lane, Boston.

EPIDERMOPHYTOSIS. A. M. Greenwood, Boston M. & S. J. **187**:176 (Aug. 3) 1922.

This is a good brief account of epidermophytosis. It not only outlines the clinical characteristics and the more usual types of treatment, but contains much of interest in regard to laboratory investigation. Considerable detail is given about the laboratory work, including the choice and examination of fresh material, with directions in regard to making culture mediums, and the growth of these organisms.

TUBERCULOUS CHANCRE. J. A. Nixon and A. Rendle Short, Brit. J. Surg. **10**:44 (July) 1922.

The writers state there is a variety of tuberculosis of the skin which so closely resembles a primary syphilitic sore that, on the rare occasions when it occurs, it is likely to be diagnosed as extragenital chancre. Hitherto, if this lesion has been recognized at all, writers have included it under the term tuberculosis verrucosa cutis, or verruca necrogenica. Since it is not a warty type of tuberculosis, however, the observer is not likely to think of a diagnosis of verruca necrogenica, and the possibility of the lesions being tuberculosis is overlooked.

Clinically, the lesion appears as a localized indurated papule, resulting from direct implantation of tubercle bacilli into the skin through a cut or an abrasion. This papule develops into a small indolent ulcer of cartilaginous consistency, having an edge that is slightly ramparted and translucent. It is attended by enlargement of the nearest group of lymphatics. Because of the induration, the ulcer is mistaken for extragenital chancre, although syphilitic chancres of the skin are usually not indurated, but assume a raspberry appearance which the tuberculous ulcer never possesses. Sometimes the tuberculous ulcer may look exceedingly like rodent ulcer, but in the latter case there is no glandular enlargement.

The writers feel that these tuberculous ulcers are due to inoculation of tubercle into persons who have a latent tuberculous infection, their tissues thus becoming intolerant to the presence of the bacilli. The ulcer at the site of inoculation represents the effort of the tissues to expel the bacilli by local necrosis.

Several case records are included. Senear, Chicago.

THE NEEDS AND DUTIES OF DERMATOLOGY. Ernest D. Chipman, J. A. M. A. **79**:419 (Aug. 5) 1922.

The needs of dermatology are defined as: (1) adequate training for those entering the specialty; (2) more knowledge of the etiology of dermatoses, and (3) more careful study of the patient from a general medical standpoint. The duties of the dermatologists of today can be summed up in the word service; service to the patient in the interpretation of the significance of his disease, service to the public in the diffusion of medical knowledge, and service to the profession in the correlation of the special knowledge of dermatologists with that of specialists in the other divisions of medicine.

EXPERIENCE WITH CHAULMOOGRA OIL DERIVATIVES IN TREATMENT OF LEPROSY. H. Morrow, E. L. Walker and H. E. Miller, J. A. M. A. **79**:434 (Aug. 5) 1922.

The authors report their experiences in the treatment of the disease with the ethyl esters of the fatty acids of chaulmoogra oil. Most of their patients

presented advanced types of the disease. Twenty-one patients were treated; two died, three became worse, five were improved, nine showed no improvement and two absconded. Treatment lasted for from three to eighteen months.

STANDARDIZATION AND PRESERVATION OF COMPLEMENT SERUM FOR THE WASSERMANN TEST. E. H. Ruediger, J. A. M. A. **79**:551 (Aug. 12) 1922.

The complement activity of guinea-pig serum can be improved by breeding of animals giving good serums, rejecting those that furnish poor serums and feeding a mixture of raw vegetables to the animals.

The fixability of guinea-pig complement was much better in winter than in summer. Frozen and salted complement serum remained active for several weeks.

A PECULIAR DISCOLORATION OF THE SKIN PROBABLY RESULTING FROM MERCURIAL COMPOUNDS (CALOMEL) IN PROPRIETARY FACE CREAMS. W. H. Goeckermann, J. A. M. A. **79**:605 (Aug. 19) 1922.

Two patients presented a peculiar slate colored pigmentation of the face and neck. Each used a face cream containing calomel. Goeckermann concluded from some experiments that the calomel was changed into mercuric oxid and mercury by the alkaline skin secretions of the patient. It is suggested that potassium cyanid in 0.5 to 1 per cent. solution should be used in similar cases.

CONTRIBUTIONS TO THE PHARMACOLOGY AND THERAPEUTICS OF IODIDS. E. D. Osborne, J. A. M. A. **79**:615 (Aug. 19) 1922.

The results of two years of study are summarized in this article. There is no striking difference in the rate of elimination of sodium iodid given intravenously as compared with that given by mouth. So far as rectal administration is concerned, it appears that a daily dose of from 2 to 3 gm. by mouth is equivalent to the maximum dose by rectum; thus it would seem that rectal administration of iodids offers no significant advantage. A dose of from 9 to 15 gm. a day by mouth divided into three equal doses is equivalent to 10 gm. in a single dose intravenously. These experiments likewise indicate that iodin given in the form of potassium iodid by mouth forms a sodium protein combination in the serum, while in the form of sodium iodid only traces of iodin enter into combination with the proteins. The question then arises as to the rôle played by the sodium protein combination in the production of iodism. It must be made the subject of further study.

QUARTZ LIGHT THERAPY IN SKIN DISEASES. E. L. Oliver, J. A. M. A. **79**:625 (Aug. 19) 1922.

Ultraviolet light has been found of special value in ulcers due to poor circulation and in port wine marks. It is of benefit in psoriasis, in localized chronic eczema, in acne vulgaris and in lupus erythematosus. It is curative in some cases of lupus vulgaris.

EXFOLIATIVE DERMATITIS FOLLOWING SILVER ARSPHENAMIN. L. Thompson, J. A. M. A. **79**:628 (Aug. 19) 1922.

The patient, who had previously been treated with arsphenamin and had developed an exfoliative dermatitis, was placed on small doses of silver

arsphenamin. He reacted with chill, fever and itching followed by a marked erythema and exfoliation. This cleared up in about two months.

WASSERMANN VARIATIONS: A STUDY OF THE SERUMS OF SEVENTY-FIVE PATIENTS BY EIGHT LABORATORIES. L. J. PALMER, J. A. M. A. **79**:724 (Aug. 26) 1922.

Three technics were used by each laboratory: (1) the usual routine test of each laboratory; (2) the routine test, but employing the same antigen, and (3) a common technic using the same reagents. In addition, the Dermatologic Research Institute cooperated, using the new technic of Kolmer.

In the untreated positive cases, the agreement with the clinical evidence was more than 90 per cent., averaging all laboratories, with a range of from 78 to 100 per cent. for individual laboratories. In cases classed as negative, the percentage of agreement varied from 88 to 97 per cent. The author is favorably impressed with the new Kolmer technic.

THE RESULTS IN FOOD ANAPHYLAXIS OBTAINED BY CUTANEOUS AND INTRACUTANEOUS METHODS: THE INFLUENCE OF ARSENICAL PREPARATIONS ON THE ANAPHYLACTIC FOOD REACTIONS. ALBERT STRICKLER, J. A. M. A. **79**:808 (Sept. 2) 1922.

There was no material difference in reactions obtained whether the cutaneous or intracutaneous methods were employed. Arsenical preparations whether administered by mouth or intravenously do not appreciably influence the endermic food tests.

SPOROTRICHOSIS. F. W. CREGOR, J. A. M. A. **79**:812 (Sept. 2) 1922.

This article contains a discussion of the disease and the report of a typical case. The patient was cured by potassium iodid internally and Lugol's solution locally.

ULCERATING GRANULOMA (GRANULOMA INGUINALE). H. GOODMAN, J. A. M. A. **79**:815 (Sept. 2) 1922.

The author's experiences with the disease in the tropics and in New York City are recounted. Tartar emetic is a specific, but it must be continued long after the lesions have disappeared to prevent recurrences.

LOCAL BLASTOMYCOSIS: REPORT OF A CASE. M. HAASE, E. R. HALL, C. H. MARSHALL, J. A. M. A. **79**:820 (Sept. 2) 1922.

The patient had a blastomycotic lesion of the cheek for twelve years, which had temporarily healed at times under iodid therapy. He developed an epididymitis, which was culturally proved to be due to blastomyces. The organism had probably spread through the blood stream.

A STUDY OF FOUR HUNDRED AND EIGHTY-FIVE CASES WITH GENITAL LESIONS. J. R. DRIVER, J. A. M. A. **79**:867 (Sept. 9) 1922.

Syphilis was found 203 times (42 per cent.); chancroids, 177 (36.5 per cent.); ulcerating granuloma, eight; erosive gangrenous balanitis and vulvitis, thirty, and the remainder of the cases were scabetic or herpetic or presented other nonspecific lesions. Of 171 chancres seen, only eight occurred in females.

THE KAHN PRECIPITATION TEST IN THE DIAGNOSIS OF SYPHILIS: A PRELIMINARY STUDY. H. L. KEIM and U. J. WILE, J. A. M. A. **79**:870 (Sept. 9) 1922.

A report is made of the test in comparison with the Wassermann test in 350 cases; approximately half of which were syphilitic clinically.

It was found that the method compares favorably in sensitiveness with the Wassermann test; over which it has the advantages of simplicity, rapidity, and reduction of sources of error. The Kahn test is superior to other precipitation tests in that the precipitate is visible to the naked eye, and there are frequent spontaneous reactions with strongly positive serums.

Further confirmatory tests, demonstrating parallelism with the Wassermann reaction, may well lead to the eventual abandonment of the latter in favor of the simpler precipitation procedure.

STUDIES IN ASYMPTOMATIC NEUROSYPHILIS. IV. THE APPARENT ROLE OF IMMUNITY IN THE GENESIS OF NEUROSYPHILIS. ALBERT KEIDEL, J. A. M. A. **79**:874 (Sept. 9) 1922.

Recent investigations have shown that invasion of the central nervous system takes place in practically all cases of syphilis. Clinically, however, it is known that less than 50 per cent. of these patients are neurosyphilitic. Immunity, treatment and pregnancy are important in the genesis of neuraxial involvement. Inefficient early treatment increases, efficient early treatment decreases, the liability to neurosyphilis. The influence of pregnancy is shown by the fact that the percentage of neurosyphilis in women who have never been pregnant approximates that of men, while in women who have conceived the incidence of neurosyphilis is markedly decreased. The formulas of Brown and Pearce for animal syphilis probably apply to the disease in humans.

FLUMERIN: A NEW MERCURIAL FOR THE INTRAVENOUS TREATMENT OF SYPHILIS; FIRST REPORT OF CHEMICAL, ANIMAL AND CLINICAL EXPERIMENTS AND RESULTS. E. C. WHITE, J. H. HILL, J. E. MOORE and H. H. YOUNG, J. A. M. A. **79**:877 (Sept. 9) 1922.

Flumerin is a synthetic organic mercurial compound containing about 32.5 per cent. of metallic mercury. After appropriate animal trials, ninety-six cases of syphilis were treated with it.

The authors do not attempt a comparative estimate of its value but their clinical impression is that the drug is superior to the soluble mercurial salts in general use by the intravenous route.

STUDIES OF BACILLUS FUSIFORMIS AND VINCENT'S SPIROCHETE. I. HABITAT AND DISTRIBUTION OF THESE ORGANISMS IN RELATION TO PUTRID AND GANGRENOUS PROCESSES. D. J. DAVIS and ISADORE PILOT, J. A. M. A. **79**:944 (Sept. 16) 1922.

There are three chief habitats of these organisms in the human body: (1) the crypts of the tonsils; (2) the teeth and (3) the smegma. Fusospirochetal organisms are found in great numbers in erosive and gangrenous balanitis. Proper hygiene of the parts which these organisms normally inhabit should greatly diminish the incidence of diseases caused by them.

A RING OF CONTACT PRECIPITATION TEST FOR SYPHILIS: A MODIFICATION OF THE KAHN TEST. R. D. Herrold, J. A. M. A. **79**:957 (Sept. 16) 1922.

A proposed modification which has the advantages of simplicity; does not require incubation, and uses very small amounts of material. Comparative tests with the Wassermann reaction and the original Kahn method were satisfactory.

A SIMPLE AID IN THE DIAGNOSIS OF SYPHILIS FROM THE PRIMARY LESION. W. D. Gill, J. A. M. A. **79**:966 (Sept. 16) 1922.

The tip and lowermost part of the barrel of an all glass syringe are removed, thus converting the syringe into a vacuum apparatus. Applied over a chancre, it facilitates withdrawal of serum for dark-field examination.

Michael, Houston, Texas.

NOTES ON A CASE OF TUBULAR LEPROSY TREATED BY INTRAVENOUS INJECTIONS OF STIBENYL. R. G. Archibald, J. Trop. Med. **24**:277 (Nov. 1) 1921.

A patient with nodular leprosy received six injections of acetyl-p-aminophenyl sodium stibiate stibenyl in doses of 0.1 gm. to 0.6 gm. during twelve days, followed by a similar course after two weeks of rest. Improvement was noted after the first course, and great benefit after the fourth course.

DHOBIE ITCH PRODUCED BY INOCULATING A CULTURE OF EPIDERMOPHYTON RUBRUM (CASTELLANI, 1909). Richard de Silva, J. Trop. Med. **24**:303 (Dec. 1) 1921.

This organism was cultured from a case of Dhobie itch, and a typical patch of the disease was produced by inoculation. The organism was recovered and cultured from the experimental lesion. No previous record of disease by inoculation from culture had been reported.

AN EXCEPTIONAL TROPICAL ULCERATION. R. W. Mendelson, J. Trop. Med. **24**:317 (Dec. 15) 1921.

Three cases are reported in which the site of inoculation developed into a small hard painless nodule which later broke down and formed a punched-out ulcer with rounded and elevated edges that tended to become undermined. The surrounding skin was inflamed and tender. Bacteriologic examination was negative for an exciting organism, but careful culturing showed a monilia growth on glucose-agar which completely prevented the growth of ordinary organisms. Ointments tended to allow the ulcer to spread and other applications were of temporary benefit. The ulcers showed a spontaneous cure in two or three months.

NOTE ON THE RECENT EPIDEMIC OF TROPICAL SEPTIC ULCER IN PALESTINE. A. G. Apostolides, J. Trop. Med. **25**:81 (April 1) 1922.

Ulcerations of this type are common to all tropical countries and were found to be clinically identical with the so-called "hospital gangrene." Most of the cases were found to be due to a fusiform bacillus and a spirochete. Ulcers were also produced experimentally by applications of membranes from

cases of "ulcero-membranous angina," and the two organisms were found in association in the membrane and also in the ulcers. Infection occurs through a break in the skin and may be spread through the medium of mosquitoes or, possibly, other insects. The incubation period is of two or three days' duration. Beginning as a papule it rapidly enlarges, becomes painful, edematous and gangrenous, with a foul odor. Usually round with undermined edges, it does not penetrate deeply. General symptoms are in proportion to the extent of the gangrene. Many forms of local antiseptic applications have been used with varying success, but the author advocates the intravenous use of neo-arsphenamin and an ointment of 20 per cent. arsphenamin. This method has given excellent results.

FRESHLY DISSOLVED TARTAR EMETIC IN VENEREAL DISEASE. F. G. Cawston, J. Trop. Med. **25**:126 (May 15) 1922.

The author believes that tartar emetic produced good results in cases of gonorrhea and chancroids, improvement being noted soon after the treatment was begun. Other methods in many cases were required to finish the treatment. In syphilis also similar results are reported.

Jamieson, Detroit.

A SURVEY OF THE EFFECT OF VENEREAL DISEASES LEGISLATION IN WESTERN AUSTRALIA FOR A PERIOD OF FIVE YEARS. R. C. Everitt Atkinson, Med. J. Australia **1**:65 (Jan. 21) 1922.

From the figures at hand, Atkinson contends that we cannot say whether venereal diseases have been on the increase or not. In the first place, we have no knowledge of the previous prevalence of the disease and, in the second place, we cannot know how much has not come to our knowledge by notification.

Regardless of whether the disease is on the increase or decrease, there is this much in favor of legislative control: the cases are treated earlier and efficaciously, and there is provision for follow-up work and education of the public, and the marriage of diseased persons is prevented.

SYPHILIS IN CHILDREN. H. Boyd Graham, Med. J. Australia **1**:265 (March 11) 1922.

This article deals for the most part with the method of injection of aqueous solution of neo-arsphenamin as performed by the author. The technic consists in the introduction of a concentrated aqueous solution of neo-arsphenamin between the iliotibial tract of the fascia lata, on the sheath of the vastus lateralis. Sixty centigrams of the drug are dissolved in 1 c.c. of sterile distilled water. After careful surgical antisepsis, the needle is inserted at an angle of 60 degrees to the skin. As soon as it is felt that the aponeurosis has been pierced, the solution is injected. The site of injection is then painted with iodin and covered with a strip of gauze. Half an hour later, the gauze is removed and the site of injection is massaged by passing the hand firmly over the site of injection in the direction of the injection. This is repeated two to three times during the ensuing twenty-four hours.

ROUTINE OF A SYPHILIS CLINIC. W. J. Beveridge, Med. J. Australia **1**:382 (April 8) 1922.

Beveridge describes the routine admission and examination of syphilitic patients in a British expeditionary hospital. He also describes a classification

of venereal sores as adopted by Major White of the British Army. The article also contains interesting statistics of extragenital sores.

POSSIBILITIES OF IRRADIATION IN MALIGNANT DISEASE. L. C. CLENDINNEN, Med. J. Australia **1**:456 (April 29) 1922.

This is an interesting and instructive article on the physics and biologic action of the roentgen rays. The article deals also with the new German cross-firing method of treating malignant growths.

GUTIERREZ, Manila.

A HISTOLOGIC STUDY OF CALCIFIED EPITHELIOMA. DUBREUILH and CAZENAVE, Ann. de dermat. et syph. **6**:257 (June) 1922.

A summary of seven cases is given, including clinical and histologic findings. It is concluded that we are dealing with an epithelioma whose cells are of a special type, viable only in the very early stages of the process, and soon undergoing necrosis, giant cells later acting as phagocytes. The element of calcification, which has been stressed heretofore, and which is suggested on palpation of the tumor, was found by the authors to be present only in fragmentary form, and its importance diminishes in their estimation.

SYPHILITIC ANGIONEUROTIC AND ANGIONEUROTROPHIC ENDOCRINIDES. AUDRY and CHATELLIER, Ann. de dermat. et syph. **6**:275 (June) 1922.

Raynaud's disease and acrodermatitis chronica atrophicans come under this heading, at least in certain cases, according to the authors, the term "endocrinide" signifying skin lesions due to endocrine disorders. In addition to the endocrinous element in the causation of these lesions, the authors believe there are also syphilitic changes in the local vessels, and the tumors of acrodermatitis chronica atrophicans are held to be syphilomas. Illustrative cases are cited, including an observation of Fordyce's.

A CASE OF SECONDARY SYPHILITIC PHENOMENA OBSERVED IN A PARETIC. MESTCHERSKY, Ann. de dermat. et syph. **6**:269 (June) 1922.

A young man who had contracted syphilis in 1911, and who had received a considerable amount of mercurial treatment and some arsphenamin without a reduction of a strongly positive Wassermann reaction, soon showed signs of paresis, which became more pronounced in 1917 and which increased until his death, in 1919. Early in 1918, he presented patches in the oral mucosa which the author diagnosed as secondary manifestations.

There is a review of the European literature on this subject.

MONILETHRIX. GOLAY, Ann. de dermat. et syph. **6**:294, 1922.

The author has made a thorough study of this condition as it appeared in a girl, aged 5 years, in whom it had been present since birth. After reviewing the literature he gives the results of his own investigations, with the following conclusions: The lengths of the enlarged portions of the hairs and of the narrowed parts are not always absolutely identical. The alternation of growth and impediment proceed with a daily rhythm, the former occurring by day, and the latter by night, as the author has clearly shown histologically. Diminution of pigment corresponds with impairment of the growth, and it therefore begins

beyond the middle of the enlarged portion, continuing up to the middle of the narrowed part, beyond which point the pigment is more plentiful as the power of growth reappears. For good reasons the author favors a theory of endocrine etiology for the condition, which may simply be an exaggeration of the normal.

AN ERYTHEMATOPAPULAR DERMATITIS IN PLAQUES, OF INTERNAL CAUSATION, DUE TO THE APPLICATION OF A VESICATORY. JEANSELME and BLAMOUTIER, Ann. de dermat. et syph. **6**:321 (July) 1922.

A woman, aged 44, presented a symmetrical eruption of papulo-erythematous plaques on the legs, forearms and buttocks, itching and burning, six days after the application of a cantharides plaster to the lumbar region. It disappeared in a week. Eruptions from the systemic effects of cantharides have never been reported, but the authors believe that in this case the possibility of other causative factors can fairly well be excluded.

THE SYPHILITIC SYNDROME OF THE INCISOR BONE. J. NICOLAS, G. MASSIA and D. DUPASQUIER, Ann. de dermat. et syph. **6**:323, 1922.

The embryology of the incisor bone is given in detail; it is destined to support the four upper incisor teeth. Syphilis often affects it, congenital syphilis giving rise to dystrophic changes, productive of Hutchinson's teeth and other dental malformations, usually limited to the incisors, and possibly also to harelip. The lesions appearing after birth, due either to congenital or acquired syphilis, are tertiary in character, the resultant tumefaction, ulceration and sinuses involving the anterior palate, the gum and the nose, the frequency being in the order mentioned. Sequestrums may be discharged, but in any case antisyphilitic treatment is to be used first, and surgery only as a matter of last resort, for the removal of lingering sequestrums and the remedy of cosmetic defects. Nineteen cases of tertiary syphilis of this bone are described, three of which were personally observed by the authors.

INTRAVENOUS INJECTIONS OF SODIUM SALICYLATE IN THE TREATMENT OF PSORIASIS. R. LUTEMBACHER, Ann. de dermat. et syph. **6**:362, 1922.

In a case of rebellious generalized psoriasis, sodium salicylate was injected daily in the dose of 3 gm. dissolved in 80 c.c. of distilled water. On the eighth day of treatment, the first improvement was noted, and after five weeks the entire eruption had disappeared. A specially purified salicylate was used.

Otto Sachs has reported a similar result (*Wien. klin. Wchnschr.*, April 21, 1921).

THE SPONTANEOUS CURE OF LICHEN PLANUS DURING THE COURSE OF DIPHTHERIA. PAYENNEVILLE and TROTABAS, Ann. de dermat. et syph. **6**:364, 1922.

In a young soldier, diphtheria supervened a few days after the onset of a generalized eruption of typical lichen planus, and the eruption rapidly disappeared, leaving no pigmentation.

PSEUDO-ELEPHANTIASTIC CONGENITAL TUMORS OF THE NUCHA. P. Noel, Ann. de dermat. et syph. **6**:366, 1922.

In an African negro soldier, aged 32, there were three cutaneous movable tumors between the nucha and the shoulders, on each side, arranged with exact symmetry. They had been present since infancy.

PRECOCIOUS MALIGNANT SYPHILIS TREATED BY BISMUTH. Tzanck, Bull. Soc. franç. de dermat. et syph. **29**:197, 1922.

At the meeting of Feb. 9, 1922, reported in a recent Bulletin, a patient was presented with a stomatitis which some thought to be due to the medication. However, it subsequently disappeared under continued treatment, and is therefore considered to have been syphilitic.

ROENTGENOGRAM SHOWING PERSISTENCE OF METALLIC DEPOSITS IN GLUTEAL REGION SEVERAL YEARS AFTER INJECTION OF UNKNOWN PRODUCTS (IODIDS OR MERCURY). C. Simon, Bull. Soc. franç. de dermat. et syph. **29**:198, 1922.

There is an illustration clearly showing the presence of aggregated opaque globules.

SERODIAGNOSIS OF SYPHILIS: FLOCCULATION PROCEDURES. Rubinstein (Leredde), Bull. Soc. franç. de dermat. et syph. **29**:201, 1922.

Various procedures, including that devised by Vernes, are reviewed and criticized. Comparative tests were made with 538 serums. The author concludes that the methods of Sachs-Georgi, Meinicke and Dold can be used only in company with the Bordet-Wassermann reaction, for their results are not always specific and their sensibility is insufficient. They cannot be used alone with safety.

PRESENTATION OF A BISMUTH COMPOUND FOR INTRAVENOUS INJECTION: THE FIRST RESULTS. Lacapere and Galliot, Bull. Soc. franç. de dermat. et syph. **29**:210, 1922.

A colloidal bismuth suspension is employed, a series of from twenty to twenty-five injections being given at the rate of three a week. The product is heated on a water-bath and then cooled before being administered. In a series of thirty cases thus treated, excellent results were obtained and the drug was well borne. Stomatitis seems to be far less frequent than with the intramuscular method, possibly because the drug is sooner eliminated when given intravenously. It is recommended for use in cases in which arsphenamin is not tolerated.

NORMAL CEREBROSPINAL FLUID IN A CASE OF PITYRIASIS ROSEA. C. Simon, Bull. Soc. franç. de dermat. et syph. **29**:210, 1922.

These findings, in one case, are presented as a matter of record.

A CASE OF GRANULOMA ANNULARE. Burnier and Rejsek, Bull. Soc. franç. de dermat. et syph. **29**:218, 1922.

The lesions in a girl aged 16 had first appeared three years previously, being located on the forearms and on the dorsum of the left hand. The

areas on the forearms, especially, were not suggestive of granuloma annulare so much as of dermatophytosis, but histologic study revealed their nature. Following the biopsies the lesions temporarily disappeared. The patient showed signs of tuberculosis.

A CASE OF LICHEN PLANUS OF THE THORAX PROVOKED BY CUPPING. BURNIER, Bull. Soc. franç. de dermat. et syph. **29**:222, 1922.

A man, aged 50, with no history of a previous similar eruption, presented himself with typical annular lichen planus lesions at sites where cupping had been performed. There was a concomitant lichen planus eruption in the oral mucosa.

RESULTS OBTAINED IN SYPHILIS BY AMINO-ARSENO-PHENOL (132). LEPINAY, Bull. Soc. franç. de dermat. et syph. **29**:222, 1922.

In a series of thirty-five cases, sixty-eight intravenous and 241 intramuscular injections were given. Intravenously, ten injections were given, at seven day intervals, a total dosage of 2 to 2.5 gm. being reached. By the intramuscular method, the intervals were four or five days, and twelve to fourteen injections were given, making a total of 2.87 to 3.5 gm. of the drug. It is apparently no more toxic than the arsphenamins, and seems quite as effective in treatment. The results from its intramuscular use are said to be fully as rapid as those following intravenous administration, although it is more slowly eliminated thus, and its intramuscular use is tolerated by those who cannot stand intravenous medication.

THE STEPS OF SYPHILIMETRY. VERNES. Travaux et Publications de l'Institute Prophylactique, Paris, Pt. 1: 1, 1922.

The author presents ten of his articles, published since 1913, dealing with the theory and practice of the serologic test which bears his name and which has been so well described by Cornwall in a recent number of the ARCHIVES (**5**:433 [April] 1922). The last article, published in the *Presse médicale* for Dec. 3, 1921, after the completion of Cornwall's paper, describes a new and superior method of measurement called "photometrie" whereby the density of the suspension is accurately measured by optical means; this supplants the colorimetric method formerly advocated.

By a thorough perusal of this publication a good working knowledge of this test should be gained. According to the author, it offers a constant reliable gage which is very helpful in controlling treatment, which is thereby rendered more effective; the patient's confidence is stimulated, and the question of permitting marriage is more readily and safely settled.

PARKHURST, Toledo, Ohio.

HISTOPATHOLOGY OF PITYRIASIS VERSICOLOR. P. A. MEINERI, Gior. Ital. mal. ven. **63**:755 (June) 1922.

Eight cases of pityriasis versicolor have been histologically studied by the author. The stratum corneum appears thickened and loosely attached to the subjacent stratum lucidum. The microsporum furfur is found only in the stratum corneum and especially in its middle and outer layers. The stratum of Malphigi presents intracellular and intercellular edema and a slight infiltration of leukocytes. In old cases some small microscopic vesicles may be

found. There is an increase of pigment in the basal layer. The corium presents a vascular dilatation, numerous proliferating cells, especially around the vessels, and granules of pigment in small groups. The article is illustrated by four photomicrographs.

THREE CASES OF SYPHILITIC REINFECTION. P. MINASSIAN, Gior. Ital. mal. ven. **63**:809 (June) 1922.

This article contains a report of three cases of a second chancre and secondary infection after apparent cure of a first attack of syphilis treated with calomel and arsphenamin.

BISMUTH PREPARATIONS IN THE TREATMENT OF SYPHILIS. A. PASINI, Gior. Ital. mal. ven. **63**:814 (June) 1922.

Pasini has used the tartrobismuthate of potassium and sodium and the citrobismuthate of sodium. Thirty-one cases of syphilis in its different stages were treated. The injections were given intramuscularly every second day, the amount of the salt being from 0.2 to 0.3 gm. to 1 c.c. of oil. A total of twelve injections comprises a course of treatment, which is followed by a second and sometimes by a third course. After the second or third dose the spirochetes disappear from the chancre and mucous patches. Healing occurs rapidly, but the papular and infiltrated lesions are somewhat slow to respond to the treatment. The Wassermann test remains positive even after several courses of twelve injections. The greatest disadvantage is the sometimes very severe stomatitis which these bismuth preparations produce. The bismuth salts are powerful spirocheticides but are inferior to the arsenicals.

THE TREATMENT OF SYPHILIS WITH BISMUTH SALTS. A. DE BELLA, Gior. Ital. mal. ven. **63**:827 (June) 1922.

The preparation used in the author's eight cases was the tartrobismuthate of potassium and sodium. He reports fairly good clinical results. The Herxheimer reaction occurred in two cases. The Wassermann test remains positive after prolonged treatment. The author concludes that the bismuth salts are useful antisyphilitics but cannot take the place of arsphenamin.

BISMUTH IN THE THERAPY OF SYPHILIS. G. DEFINE, Gior. Ital. mal. ven. **63**:834 (June) 1922.

The tartrobismuthate of sodium and potassium was useful in a case in which arsenic and mercury had failed. There was no improvement in a case of paresis.

SYPHILITIC FEVER. Z. ARMANDO, Riforma med. **38**:697 (July) 1922.

Syphilitic fever may appear during the secondary stage of the disease and is probably a toxic phenomenon. It may occur in the late or tertiary stage, usually in connection with visceral or nervous syphilitic disease. It may be intermittent, continuous or irregular. The author reports a case with localized bronchopneumonia, hypertrophy of the spleen and liver and intermittent fever of malarial type. The Wassermann test was strongly positive. The patient made an uneventful recovery under mercury and arsphenamin.

PROPHYLAXIS OF ARSPHENAMIN ACCIDENTS. A. Fontana, Riforma med. **38**:699 (July) 1922.

Fontana considers the injection of epinephrin superior to atropin and to the previous injection of a small amount of the arsenical, in the prevention of arsphenamin reactions. He advises thoroughly mixing the blood with the solution in the syringe and injecting very slowly. In cases of malignant syphilis and when there is intolerance to the drug, the previous application of mercury may avoid serious reactions. He considers the Milian sign (arsenical conjunctivitis) of value as indicative of impending trouble if more arsphenamin is used.

MALIGNANT LYMPHOGRANULOMA. G. Castaldi, Riforma med. **38**: 795 (Aug.) 1922.

Since 1898, when Sternberg described this disease of the hemopoietic system the opinions have been divided as to its etiology; some believing that the condition is due to tuberculosis, while others believe that it is caused by an undetermined virus. The author reports two cases of typical lymphogranulomatosis with Sternberg cells in the glands and the spleen and small granular infiltrations of the liver. No trace of tuberculosis could be found in these cases. Bacteriologic examinations and experimental inoculations in animals were all negative for Koch's bacilli. Castaldi concludes that "the epidemiology, the pathology, the clinical and the experimental pathology are against its tuberculous nature and that malignant lymphogranuloma is a morbid entity with a definite clinical physiognomy."

A CASE OF EARLY SEVERE SYPHILIS. Italo Levy, Riforma med. **38**: 800 (Aug.) 1922.

Report is made of a case of serpiginous ulcerations of the face and destruction of the soft palate. The destructive lesions appeared ten months after the chancre. The patient had no specific treatment before.

RECKLINGHAUSEN'S DISEASE. M. Acuña and F. Bazan, Prensa med. Argentina **9**:12 (June) 1922.

Two cases of this disease are reported in children 11 and 12 years of age, respectively. In the first case there was a history of hereditary syphilis, positive Wassermann reaction and symptoms of hypothyroidism. The second patient was mentally defective. The authors think that Recklinghausen's disease may be the result of certain endocrine disturbances.

Pardo-Castello, Havana, Cuba.

A CASE OF PITYRIASIS AMIANTACEA. B. Ludovici, Dermat. Wchnschr. **74**:153 (Feb. 18) 1922.

A case of this rare and severe form of seborrhea sicca capitis is described, in which, besides the familiar minute scale formation, the shedding of the entire follicular orifice occurs, in such a manner that the latter is taken along as a cuff by the hair in its growth. Some of these cuffs rise as high as 2 mm. above the level of the scalp.

REPRESENTATION OF SCHREUS REGARDING THE AUTHOR'S INVESTIGATIONS OF STOMATITIS MERCURIALIS ULCEROSA. J. Almkvist, Dermat. Wchnschr. **74**:155 (Feb. 18) 1922.

The author contradicts statements ascribed to him by Dr. H. Schreus, in an article entitled, "A Way to Prevent and Treat Mercurial Stomatitis" (*Dermat. Wchnschr.* **73**:1270, 1921). The bacteria which are causative factors in ulcerative mercurial stomatitis and colitis are not specific micro-organisms, but various putrefactive forms. Their rôle is fulfilled in two ways: first, by a local erosion from hydrogen sulphid, and second, by local resorption, producing together with the mercury in the connective tissue, a connective tissue necrosis. The mercury in the walls of the capillaries is precipitated intracellularly as mercuric sulphid by action of the resorbed hydrogen sulphid. The author recommends disinfection of all bacterial foci in the buccal cavity as the best prophylactic procedure.

TREATMENT AND PREVENTION OF MERCURIAL STOMATITIS. F. Hammer, Dermat. Wchnschr. **74**:158 (Feb. 18) 1922.

The author recommends from 10 to 20 per cent. of chromic acid applied to the teeth, gums and tonsils with a wooden applicator. Although the treatment is painful, it effectually destroys the putrefactive micro-organisms causing the affection.

MULTIPLE SKIN LESIONS IN FUNCTIONAL ANESTHESIA. E. Pick, Dermat. Wchnschr. **74**:177 (Feb. 25) 1922.

The fact that multiple ulcers occur in nervous and hysterical persons under the aspect of neurotic gangrené, is well recognized; but the question whether the lesions are spontaneously trophoneurotic or artificially produced, is frequently difficult to answer. A case is described occurring in a middle-aged man, who was burned with hot metal on the dorsum of the right hand during routine work in an iron foundry. An ulcer resulted which required three months to heal. Two weeks after the healing was complete, erythematous spots appeared on the forearm. These later became vesicular and ulcerated. There was an accompanying complete anesthesia for touch, pain and temperature of the right arm and hand. This anesthesia and the skin lesions disappeared quickly after slight faradization.

A CASE OF LEUKODERMA IN PITYRIASIS LICHENOIDES CHRONICA. J. Almkvist, Dermat. Wchnschr. **74**:201 (March 4) 1922.

Pityriasis lichenoides chronica (Juliusberg) or dermatitis psoriatiformis nodularis (Neisser-Jadassohn), as well as syphilis, psoriasis, and seborrheic eczema, produces leukoderma. A case is described in which the leukodermic spots were generalized and appeared on the sites of the preceding eruption of pityriasis lichenoides chronica.

TECHNIC OF EMPLOYING RADIUM AND MESOTHORIUM IN DERMATOLOGY. W. Brinckmann, Dermat. Wchnschr. **74**:204 (March 4) 1922.

The following factors form a basis for technic: The quantity of the radium or mesothorium expressed in milligrams of radium bromid: (1) the extent of

surface which is covered by this quantity, (2) the kind and thickness of the filter, (3) the duration of the exposure, and (4) if the first three factors are constant, the last is simply a matter of experience.

A CASE OF UNILATERAL LINEAR PSORIASIS. J. STANGENBERG, Dermat. Wchnschr. **74**:210 (March 4) 1922.

The case is described with illustrations, the eruption being segmentally arranged in a manner simulating herpes zoster.

A NEW ELECTRICAL ACCESSORY APPARATUS, "WIGOSTAT TRANSFORMER." T. BENEDEK, Dermat. Wchnschr. **74**:225 (March 11) 1922.

The apparatus consists of an oxidized wire resistance, rolled on porcelain and polished at its points of contact. Along these, bilaterally arranged, and located in the middle third of the wire, are two sliding springs which may be approximated or separated by means of a spindle with halves of opposite winding. In this manner the length of the resistance wire between the sliding springs may be continually changed. The two springs are connected by metal with two clamps on the outside of the apparatus. In addition the beginning and end of the entire resistance wire lead to two clamps carefully insulated by hard rubber.

THE BILIRUBIN CONTENT OF BLOOD SERUM DURING TREATMENT WITH MERCURY AND ARSPHENAMIN. P. SCHNEIDER, Dermat. Wchnschr. **74**:228 (March 11) 1922. (*Continued.*)

After numerous investigations, the author concludes that the bilirubin content is increased in nearly all cases at the beginning of treatment, but that it approaches normal as the treatment progresses.

THE BILIRUBIN CONTENT OF BLOOD SERUM DURING TREATMENT WITH MERCURY AND ARSPHENAMIN. P. SCHNEIDER, Dermat. Wchnschr. **74**:250 (March 18) 1922. (*Concluded.*)

Further investigations support the conclusions given in the preceding article. A disturbance of the functions of the liver by the disease or its treatment may account for the augmentation of the serum bilirubin.

COMBINED PRECIPITATION (SIMULTANEOUS SACHS-GEORGI-MEINECKE REACTION). STERN and EVENING, Dermat. Wchnschr. **74**: 235 (March 11) 1922.

For the mixture of both extracts distilled water is used as follows (0.5 Sachs-Georgi reaction plus 0.5 Meinecke reaction plus 5.0 distilled water), while the serums are diluted with 2 per cent. sodium chlorid solution. To 0.2 inactivated serum add 0.8 of 2 per cent. sodium chlorid; shake well; add 0.5 cm. of the extract mixture; let it stand for two hours in the water-bath and eighteen hours at room temperature, and read in agglutinoscope.

An examination of 1,500 serums was made. As some Wassermann positive syphilitic serums did not give precipitation, negative precipitation reactions were considered indeterminate.

CUTIS GYRATA OF THE FOREHEAD. A. STUEHMER, Dermat. Wchnschr. **74**:249 (March 18) 1922.

The patient, a boy aged 19, had noticed the gradual development of the condition since he had a trauma ten years before. Simultaneously a similar lesion evolved on the occiput. They were asymptomatic. All other findings were normal. There was a deep sagittal furrow between two convolutions on the forehead with symmetrically arranged furrows and convolutions on either side of it. Some of these did not follow the natural lines of wrinkling produced by muscular action.

DERMATITIS FROM SUBSTITUTES FOR TURPENTINE. GALEWSKY, Dermat. Wchnschr. **74**:273 (March 25) 1922.

Four cases of occupational dermatitis in painters due to the use of substitute products for turpentine are reported. There were no unusual features in the eruptions.

MULTIPLE SOFT WARTS OF THE BUCCAL MUCOSA. E. STERN, Dermat. Wchnschr. **74**:274 (March 25) 1922.

Numerous rounded, pinhead sized soft verrucae were present on the inner surfaces of the lips and in the corners of the mouth of a 14 year old girl. There were no other warts on other parts of the body.

CHANCRE OF THE URETHRA. G. GJORGJEVIC, Dermat. Wchnschr. **74**: 276 (March 25) 1922.

Six cases of intra-urethral chancre are presented. Five were in men and one was in a woman. The findings were confirmed by dark-field examination.

THE CAUTERY NEEDLE AS A THERAPEUTIC AND COSMETIC INSTRUMENT. A. POKORNY, Dermat. Wchnschr. **74**:297 (April) 1922.

This instrument is recommended for the treatment of telangiectases, nevus flammeus, angiomas and small pigmented nevi on the face. The author says that keloids do not appear subsequent to this method of treatment.

MY ACTIVATED WASSERMANN METHOD IN SYPHILIS. H. HECHT, Dermat. Wchnschr. **74**:300 (April) 1922.

A description of the author's technic and results is presented, using an activated serum.

ANDREWS, New York.

SYPHILITIC ORCHITIS SIMULATING A NEW GROWTH. M. ZEISSL, Wien. klin. Wchnschr. **34**:583, 1921.

This is a report of a patient who had been under observation for a number of years. The differential diagnosis of syphilitic involvement of the testicle and new growth is given.

CONSIDERATION OF THE INTRAVENOUS TREATMENT OF PERSISTENT PRURITIC DERMATITIS. MAXIMILIAN STRASSBERG, Wien. klin. Wchnschr. **34**:595, 1921.

In addition to numerous local applications, the author has found the intravenous introduction of autoserum effective. About 100 c.c. of blood are drawn from the vein, allowed to remain at room temperature for three or four hours.

and then kept in the icebox for from twelve to twenty hours. The serum is reinjected about twenty-four hours after it had been withdrawn. The injection is repeated at intervals of three or four days. Urticaria, weeping eczema and pruritus senilis have been influenced favorably by this treatment. In addition to autoserum therapy, the use of whole blood has been given a trial In every instance there has been marked relief when this procedure was tried in cases of itchy diseases of the skin. Blood was also withdrawn up to 100 c.c., and replaced with physiologic sodium chlorid solution, but the result was poor. The question of ions in the blood and their effect on the nerves must be considered in this regard.

SECOND INFECTION WITH SYPHILIS WITHIN FIVE YEARS OF THE CURE OF THE FIRST BY STERILISATIO MAGNA. MAXIMILIAN ZEISSL, Wien klin. Wchnschr. **34**:596, 1921.

A student was infected with syphilis in July, 1910. *Spirochaeta pallida* was demonstrated and the Wassermann reaction was positive. He received but one dose of arsphenamin intramuscularly. No secondaries were observed up to July, 1911, despite inspection every other day. The Wassermann reaction was last positive late in 1910. In 1915, the reaction was negative. In January, 1915, after an incubation period of eight weeks, the patient reported with a new infection. *Spirochaeta pallida* was found and the Wassermann reaction was positive. One injection of arsphenamin intramuscularly did not inhibit the secondaries. Despite other treatment, the course of syphilis with this infection was extended.

A NEW METHOD OF INJECTING TUBERCULIN IN WIDESPREAD SKIN TUBERCULOSIS. MAXIMILIAN STRASSBERG, Wien. klin. Wchnschr. **35**:54 (Jan. 19) 1922.

The author uses the dose of O. T. (old tuberculin) to be injected, but dilutes it so as to permit multiple injections locally about the lesions of tuberculosis of the skin. The local reaction of the introduced O. T. has about fifty sites of injection at which to act, and in addition the general reaction need not be different from that of the same dose injected at one place. Of course, only a part of the sum total of reactions can be produced at any one site of injection of the diluted O. T.

IS THERE AN ACTUAL NATURAL RESISTANCE TO SYPHILIS? OBSERVATIONS ON PROSTITUTES. ROBERT BRANDT, Wien. klin. Wchnschr. **35**:223 (March 9) 1922.

A study of a group of prostitutes for a period of years has shown that, despite every possibility of infection, some of them did not become infected with syphilis until many years of their professional life had elapsed. In the interim, repeated examinations had disclosed no lesions nor serologic evidence of the disease. The women were of the lowest level of professional prostitutes and had undoubtedly been exposed repeatedly to infection.

REMARKS CONCERNING THE CONTRIBUTION OF BUSACCA, ENTITLED, "A NEW INTRACUTANEOUS REACTION IN SKIN TUBERCULOSIS." VJEKOSLAV KUSAN, Wien. klin. Wchnschr. **35**:248 (March 16) 1922.

The use of horse serum for the diagnosis of tuberculosis in human beings is held not to be a reliable test. Such positive reactions as have been reported are conceived to have been due to trauma.

REPLY TO THE REMARKS OF DR. KUSAN. Attilio Busacca, Wien. klin. Wchnschr. **35**:248 (March 16) 1922.

The number of cases on which Kusan bases his conclusions is too small for definite ideas. The factor of traumatism has been properly controlled by injection of warm Ringer's solution in a series of cases taken from Finger's clinic. There were three positive results among forty-one patients with various diseases of the skin. It is interesting that the diagnosis of these three included two cases of lupus vulgaris, and one of lupus erythematosus.

CONTRIBUTION TO THE STUDY OF DERMATITIS OF ARSPHENAMIN OR MERCURY OCCURRING DURING THE TREATMENT OF SYPHILIS. Josef Klaar, Wien. klin. Wchnschr. **35**:266, 1922.

In the five-year period of 1916-1921, thirty-four cases of dermatitis due to arsphenamin or mercury have been observed, of which five were brought to the hospital after having treatment elsewhere. There were nineteen patients who had combination mercury and arsphenamin courses; two patients who had had only silver arsphenamin; three patients who had had injections of neo-arsphenamin only; and ten who had had injections of mirion and neo-arsphenamin. The mirion-treated patients, who did not receive arsphenamin, never showed any dermatitis; hence the author absolves this drug from being the cause of the dermatitis. In addition to the classic dermatologic picture, many patients presented edema of the face, loss of weight, hemorrhages, stomatitis, albuminuria, alopecia, enteritis, vulvitis, pyoderma, melanoderma, paronychia, conjunctivitis or pneumonia. The secretion of sweat and sebum is diminished. The loss of hair and nails that may occur is probably due to some disturbance of internal secretion, as evidenced by the occurrence also of disturbances of menstruation.

In individual cases, it is impossible to determine whether the mercury or the arsphenamin has caused the ill-effects.

CONTRIBUTION TO THE STUDY OF ARSPHENAMIN AND MERCURY DERMATITIS OCCURRING DURING THE TREATMENT OF SYPHILIS. Josef Klaar, Wien. klin. Wchnschr. **35**:297, 1922. (*Concluded.*)

A number of cases came to necropsy. In general, it may be said that failure of the heart could be the cause of death. Pneumonia may have been a complication in a youthful individual who died, but he also showed a degenerated heart muscle. Necrotic inflammatory changes in the small and large intestine was present in another case. The mechanism of the dermatitis has not been unfolded by the necropsy studies. The parenchymatous changes of the liver, thought possibly to be of etiologic significance, can just as readily be secondary changes. Patients who have passed through a severe dermatitis may have the Wassermann reaction reversed to negative, and may show no symptoms of syphilis later. The reports of some authors on the favorable influence of fever-exciting injections (milk, typhoid vaccine) are similar in this respect. It is noted that the number of women with dermatitis was about five times greater than the number of men.

EDEMA OF THE TONGUE AFTER MIRION INJECTIONS. N. Nander. Wien. klin. Wchnschr. **35**:296, 1922.

A patient with tabes dorsalis, after numerous courses of mercury and arsphenamin was put on a course of mirion and arsphenamin. After a num-

ber of injections of both, his tongue became so edematous that he was unable to talk or eat. The edema did not encroach on the glottis, but did spread to the submaxillary regions. Although the aspect seemed grave enough, within two hours the parts became normal in size, and the edema had disappeared. Although the patient has since received a number of neo-arsphenamin injections, no sign of the edema has returned. It is thought that this swelling was a sign of severe iodism.

EXPERIMENTS WITH SODIUM NUCLEINATE IN THE TREATMENT OF PARESIS WITH MALARIA. HEINRICH KOGERER, Wien. klin. Wchnschr. **35**:342, 1922.

In the treatment of paresis at the Vienna Psychiatric Institute with the injection of malarial parasites, one had to determine a cure of the malaria before discharging the patients. After tests of the blood had been negative following treatment of the induced malaria by quinin and neo-arsphenamin, the blood was examined after roentgen irradiation of the spleen. Later, the use of injections of sodium nucleinate, 5 c.c. of a 10 per cent. solution, was found to be more efficacious. In a series of twenty-five patients, three gave positive blood smears after this injection, and continued treatment of the experimental malaria was instituted. It has been shown, too, that experimental malaria is much easier to cure than the malaria ordinarily induced by the bite of the anopheles.

PRACTICAL EXPERIENCE WITH THE SIGNIFICANCE OF THE GUM BENZOIN REACTION ON THE CEREBROSPINAL FLUID. FRITZ MARS, Wien. klin. Wchnschr. **35**:417, 1922.

This reaction is to be recommended as it is cheap, easy of preparation and, in a series of cases, has seemed of value in the determination of disease condition. The reaction has been paralleled with the gold sol reaction. The report of this experiment is in course of preparation.

A NEW INTRACUTANEOUS REACTION IN SYPHILIS. ATTILIA BUSACCA, Wien. klin. Wchnschr. **35**:523, 1922.

During his experiments with horse serum intracutaneous reactions in tuberculosis, the author made some experiments with gelatin in the same way. A 10 per cent. sterilized solution of gelatin (Merck) was used. In tuberculosis, the positive reaction was present in only 45 per cent. of the cases, a percentage too small to be of use in diagnosis. In syphilis, on the contrary, 71 per cent. of the patients gave a positive reaction with the gelatin, and the patients in the primary stage, sclerosis without exanthem, gave a positive reaction in twenty-seven of twenty-nine instances. The Wassermann reaction was positive in only twenty of this series. In the secondary cases, however, the gelatin reaction was positive in only ninety-five of 149 cases, and the Wassermann reaction was positive in all except nine.

If the horse serum reaction and the gelatin reaction were positive in the same case, the diagnosis of tuberculosis was assured.

The value of the test in early primary syphilis seems to be great, especially in the light of the possibility of abortive treatment.

GOODMAN, New York.

PUNCTURE OF GLANDS AND ITS SIGNIFICANCE IN THE DIAGNOSIS OF SYPHILIS. V. SEDLAK, Ceska dermat. **3**:201, 1922.

Puncture of indurated glands resulted in the finding of spirochetes in fifty out of fifty-two cases examined during the primary stage, and in eighteen

out of twenty-one cases in the secondary stage. The puncture seems to be of great diagnostic significance, especially in cases of chancres negative for spirochetes—treated or inaccessible (phimosis)—and while the Wassermann reaction is yet negative. A positive gland puncture may decide the diagnosis in time for abortive treatment.

EXPERIMENTS ON DIFFUSION OF COMPLEMENT. J. KABELIK, Ceska dermat. **3**:211 and 233, 1922.

To study the conditions which influence the diffusion of complement the author superimposed various strengths of complement in the test tubes on thin agar (1 to 0.125 per cent.) to which he added as indicator highly sensitized red corpuscles. His experiments led to the following results: The more concentrated and stronger was the complement, the more sensitized were the corpuscles, the smaller was the number of corpuscles used and the less concentrated was the agar, the greater was the thickness of the hemolyzed layer. The diffusion of complement was the most rapid at the beginning of the experiment; it became slower rapidly and ceased on the third day by inactivation of complement. Analogous experiments on the diffusion of other substances tend to lead to the opinion that the colloid particles of proteins which carry the complement quality of serum are larger in colloid particles of simple serous proteins.

CUTANEOUS TUBERCULIN REACTIONS IN SKIN TUBERCULOSIS. K. HUBSCHMANN, Ceska dermat. **3**:246, 1922.

The author obtained a positive cutaneous reaction in forty-five cases of various forms of skin tuberculosis (thirty-two of lupus vulgaris). His experiences disagree with the statement of Wolff-Eisner that in lupus a negative reaction is relatively common. Curshmann found more cases giving a positive reaction with bovine tuberculin than with human virus, while Kretschmer's experience was just the reverse. The author did not have a single case giving a positive reaction with one tuberculin and a negative one with the other.

INTRAMUSCULAR INJECTIONS OF NEO-ARSPHENAMIN "GLUCO 914" IN THE TREATMENT OF SYPHILIS. A. MESKA, Ceska dermat. **3**:250, 1922.

This preparation put up by Robert and Carrière, Paris, is recommended for cases in which for some reason or other the intravenous injection cannot be used. The neo-arsphenamin is dissolved in glucose and comes in convenient syringe ampules ready for use. The method is simple and almost painless. Good results of treatment combined with mercury are reported.

PRIMARY CHANCRE OF THE EYELID. PROFESSOR DEYL, Ceska dermat. **3**:258, 1922.

A young pregnant woman (five months) presented a painless, cartilaginous, purple-red induration of the right upper eyelid with papulosquamous brownish red lesions on the forehead, falling out of the eyebrows and lashes. The Wassermann reaction was four plus. Genital examination was negative for syphilis. There were no traces of other primary syphilitic lesions on the body. The unusual features of this case are: (1) the lack of a typical primary ulcer—the lesion on the eyelid being without ulceration, and (2) the lack of submental or preauricular adenopathy; there were a few enlarged posterior

cervical glands and one above the clavicle. The findings cleared up in four months under combined treatment. The patient gave birth to a healthy child. The article contains a detailed differential diagnosis, especially the exclusion of tarsitis syphilitica.

EXPERIENCES WITH THE DOLD PRECIPITATION REACTION. M. DZINBAN, Ceska dermat. **3**:273, 1922.

The author used Dold's original technic in 600 cases and compared the results with those of the Wassermann and Sachs-Georgi reactions. They ran parallel in 92.83 per cent. of cases; in 98.16 per cent. Dold and Sachs-Georgi agreed; Wassermann and Dold reactions agreed in 90 per cent. on early reading and in 93.3 per cent. on late reading of precipitation. To shorten the time of the reaction the author in some cases centrifuged the serum and the antigen, which had been previously incubated from one to two hours. In strongly positive cases the results could be interpreted in five, ten or fifteen minutes. When results were doubtful the author added the complement and the hemolytic system to settle the question, as according to Gaehtgens and Salvioli only specific precipitates hinder hemolysis.

SPINKA, St. Louis.

Society Transactions

MINNESOTA DERMATOLOGICAL SOCIETY

Annual Meeting, Aug. 5, 1922

JOHN BUTLER, M.D., *Chairman*

URTICARIA PIGMENTOSA. (From the University Clinic.) Presented by DR. MICHELSON.

A baby, aged 4 months, for the last two and a half months had shown a yellowish and brownish-yellow macular eruption located on the trunk and face. The lesions varied in size from 0.5 to 0.75 cm. in diameter. There was no scratching, therefore it was concluded that the lesions did not itch. The baby gained steadily in weight and its general health was perfect. Rubbing the lesions produced some edema. There was no marked dermographismus. Biopsy revealed a slight infiltration in the papillary layer. A few mast cells were noted in the infiltrate, but the infiltrate was not pure mast cells.

MILTOY'S DISEASE. Presented by DR. MICHELSON.

Miss F., aged 19, born in Minnesota and never out of the state, whose general health was excellent, said that since birth the left leg had been much larger than the right. It had never been painful except when injured, and then it healed slowly. She said that no other member of her family was afflicted with the same condition. On examination it was noted that the left leg was 4 inches (10.16 cm.) greater in circumference than the right at the middle of the calf, and that the swelling was of a doughy character and did not pit on pressure. The enlargement extended to the groin. There was no history of febrile attacks or of general disturbance.

CHELITIS GLANDULARIS APOSTEOMATOSA. Presented by DRS. BUTLER and ODLAND.

A man, aged 74, a retired paint merchant, had had this condition for eight years. The lower lip was greatly thickened, edematous and everted, and studded with hemp seed size glistening drops of secretion which had formed at the orifices of the mucous glands. He gave a history of chronic nasal catarrh.

A CASE FOR DIAGNOSIS (HYPODERMATIC NODULES). (From the University Clinic.) Presented by DR. MICHELSON.

Mr. M., a tailor, aged 46, married, who had no children or history of miscarriage in the family, said that he had had a penile sore twenty-five years ago. There was no history or signs of syphilis. Six months before he developed two nodules under the skin in the region of the right thigh. They became painful and after two months discharged pus for several weeks; they have since healed completely, leaving ordinary scars. The scars did not sug-

gest those which follow gumma. During the last four months several other nodules have developed in the same region. The nodules were apparently deep in the hypoderm and freely movable, and were more easily discerned when the patient was standing erect. They seemed to disappear when he was lying on his side. The periosteum over the trochanter was thickened and rough, but the nodules were not adherent to the bone. Biopsy revealed a chronic, rather diffuse, infiltration of the hypoderm, which was not characteristic of either tuberculosis or syphilis. There was a marked thickening of the blood vessel walls and a profuse polymorphous infiltrate about the vessels and in the pars adiposa. The Wassermann test was negative. The patient was reported for clinical diagnosis of the tumors mentioned.

DISCUSSION

DR. ORMSBY: I worked for some time in London, and during that time we did a great deal of work among tuberculous children. One type of lesion was characterized by a subcutaneous nodule which enlarged, ulcerated and discharged. Then it would heal and a new nodule would form, and the process would be repeated. Before I saw the slide or Dr. Michelson's diagnosis, I had decided that this was a case of scrofuloderma.

In relation to tuberculosis of the hypoderm of Wende, I think that it shows that Wende's case may have been a sarcoid.

DR. MICHELSON: Scrofuloderma is a frequent form of tuberculosis of the skin, especially in children. It is often seen in the European clinics. It begins with a deep nodule in the cutis without signs of inflammation, gradually extends into the skin, becomes bluish red, softens and ulcerates. It may originate in glands, bone or the lymphatics of the hypoderm. The nodular tuberculosis as described by Wende is a different condition. In the treatment of tuberculosis of the skin one must take into consideration the type with which we are dealing, whether it is primary or secondary; the prognosis is also guided by the classification.

SCROFULODERMA COLLIQUATIVA. Presented by DR. SWEITZER.

A. G., a woman, aged 38, single, born in the United States, was seen in April, 1922, with a soft, easily bleeding patch on her right cheek. The patient said that she had had abscess glands in the neck when 16 years old. The present illness started in August, 1921, with the appearance of a small papule on the cheek. The disease spread slowly, and in October, 1921, the patch was the size of a dime. She had been treated with the sun lamp with no apparent benefit. A section taken in April, 1922, showed tuberculosis. Treatment with acid mercuric nitrate was started, and healing has been rapid.

KERATODERMA MACULOSA SYMMETRICA PALMARIS AND PLANTARIS. Presented by DR. SWEITZER.

M. A., a woman, aged 33, was seen in June, 1922. The patient had numerous small, hard, horny, papular lesions on the palms and soles. The palms were not as extensively involved as the soles; there were numerous small, yellow, horny papules on both heels. Many of the lesions had a small central depression. The condition on the palms and soles had been present since childhood, and the patient's father and one brother were similarly affected.

EPITHELIOMA OF THE CHEEK IN LUPUS ERYTHEMATOSUS SCAR AND ACTIVE LUPUS ERYTHEMATOSUS VISCOIDES OF HANDS. (From the University Clinic and General Hospital Service.) Presented by DR. MICHELSON.

A man, aged 64, born in Sweden, said that he had had a chronic scaling disease of the skin confined to the scalp and face since he was a young man, that he had received various kinds of treatment, including roentgen-ray and radium treatment, that a growth had developed on the right ear which a physician called cancer and for which he removed the right ear lobe eight years before. During the last year he had developed two elevated hard circumscribed growths on the cheeks within the scar which followed his previous disease. The patient had a typical lupus erythematosus scar of the scalp and face and an active chronic lupus erythematosus on the back of his hands. Two circumscribed hard pearly bordered growths were noted on the right cheek which had developed within the scar, and which had been diagnosed as epithelioma.

CHEILITIS EXFOLIATIVA. Presented by DRS. BUTLER and ODLAND.

A boy, aged 14, presented an eruption on the lower lip of several years' duration. The mucous membranes of the lower lip showed several small, dry areas covered with adherent scales and crusts. At times he had noticed improvement followed by exacerbations.

A CASE FOR DIAGNOSIS. Presented by DRS. BUTLER and ODLAND.

A woman, aged 42, presented extensive mucous membrane lesions of the mouth of four months' duration. She said that the lesions first appeared on the right buccal cavity and rapidly spread to other parts until it involved the inside of the cheeks, the gums, the ventral surfaces and margins of the tongue, the posterior pharynx and fauces. The lesions were grayish white, fairly sharply marginated and raised, giving the appearance of a raised membrane which when detached showed a bleeding surface. Microscopic examination failed to show any mycelia or yeastlike elements. A forty-eight hour old culture showed no growth.

GUMMA FOLLOWING TRAUMA. Presented by DR. OLSON.

Mrs. W., aged 49 years, showed bilateral gummas at the sites of the patellar bursas. Four months previously she had fallen on the ice. The injury was followed by ecchymoses below both knees. These bruises did not heal but gradually became ulcers. At the time of presentation the patient had received four arsphenamin injections, and the gummas were almost healed.

DYSPITUITARISM WITH HYPERHIDROSIS. Presented by DR. OLSON.

A boy, aged 14, was first seen eight months ago, when he complained of excessive sweating of the feet. His muscles were well developed and firm. He complained, however, of exhaustion after moderate exertion. He had been unable to take part in such sports as skating. He suffered from severe headaches. The axillary spaces were free from hair, and the pubic hair was feminine in arrangement. Local application of formaldehyd in alcohol and thyroid administered internally had resulted in relief from the hyperhidrosis and improvement in the general condition. The headaches were less frequent and severe, and there was less fatigue after exertion.

RESISTANT THRUSH. Presented by DR. OLSON.

A girl, aged 8 years, was presented at the last annual meeting. The diagnosis had been confirmed by culture. The thrush had not responded to treatment continued over a period of four years. The tongue and mouth showed the white patches of thrush.

LICHEN PLANUS, VERRUCOUS AND ATROPHIC. Presented by DR. SWEITZER.

R. H., a woman, aged 40, had an eruption which had been present since she had been vaccinated fifteen years before. At first the eruption was general, but after several months it disappeared, with the exception of a few patches on the knees. The left wrist showed typical lichen planus lesions. The right wrist showed a circular lesion resembling a granuloma annulare. On the right tibial region was a round verrucous lesion, and over the region of the knee joint were two irregular atrophic lesions.

PSORIASIS. Presented by DR. SWEITZER.

M. B., a man, aged 41, presented a verrucous eruption on the thumb and two middle fingers of the left hand and the thumb and third finger of the right hand. The disease had been present for nearly two years, alternately improving and becoming worse. The patient had been treated for eczema of the hands by two physicians. A typical patch of psoriasis was present on the elbows.

DISCUSSION

DR. FREEMAN: When I first saw this case I thought it was psoriasis, but I am now inclined to doubt it. I believe that an epidermophyton infection should be considered.

SCROFULODERMA. (From the General Hospital Service.) Presented by DRS. MICHELSON and ODLAND.

Mrs. H., a widow, aged 38, who had no children, with a blood Wassermann test repeatedly negative and no history of syphilis, presented herself on account of a rather extensive lesion of the region of the right wrist. She said that two years before she developed a swelling just over the back of the hand, which gradually enlarged and after two months discharged a slight amount of pus. In four weeks this swelling subsided; then another similar swelling developed 4 cm. higher on the wrist. She treated it with hot poultices, but it did not break down. A physician made an incision, and the lesion discharged pus for fifteen weeks. He then burned it with a caustic stick. In March, 1921, new lesions, numbering about five, developed subcutaneously and gradually enlarged until they were the size of a hazelnut. The skin over the nodules was red and slightly painful. The nodules appeared to be adherent to the skin and were closely attached to the underlying tissues. There were no sinuses. Biopsy revealed a deep seated granulomatous structure with typical tubercle formation. Staining for tubercle bacillus was negative. Animal inoculation had been performed, but too recently for report. This condition was apparently scrofuloderma developing in the lymphatics of the hypoderm.

INTERTRIGO INTERDIGITALIS SACCHAROMYCETICA. (From the University Clinic.) Presented by Drs. Michelson and Odland.

A woman, aged 60, had had a disease of the skin between the fingers for the last eight years. It consisted of moist, white lesions located in the interdigital spaces of both hands. The epidermis was accumulated into a mass of undermined, sodden, white, soft débris. It was rather easily removed, and Dr. Odland recovered a saccharomyces from the scrapings, which were easily cultivated. The condition has been refractory to ordinary treatment. The microscope shows finger granules.

NEUROTIC EXCORIATIONS. Presented by Dr. Michelson.

Miss B., aged 76, has for the last four years had lesions on the face, accompanied by an irresistible desire to dig into them. This she had done after retiring. When oozing was produced the desire subsided. There had been no effort to deceive nor any play for sympathy. She simply said that the lesions developed as little bumps and the excoriations were produced and healed by scarring. She showed numerous excoriations and scars on the face and forearms.

IDIOPATHIC MACULAR ATROPHY. Presented by Drs. Butler and Odland.

A woman, aged 21, said that the eruption had been present for three years and that it began as small, slightly reddish spots which, following scaling, became lighter in color. It first involved the neck and shoulders and gradually spread to the upper part of the trunk and lumbar region. When first seen the lesions were atrophic patches, oval in shape, varying in size from that of a split pea to that of a finger-nail. The skin was smooth, thin, wrinkled and white. The lesions appeared to be slightly depressed.

A CASE FOR DIAGNOSIS. Presented by Dr. Armsrong.

J. W., a boy, aged 14, who was first seen April 18, 1921, and at that time presented numerous lesions of a type similar to those now present, gave the following history: He was vaccinated June 30, 1921. This was followed by a rather severe local reaction and the formation of the lesions contiguous to the site of inoculation; afterward the lesions spread to other parts. Until April 18 there had been twenty-seven in all. A Wassermann test had been made before I saw him, and although it was negative, arsphenamin, mercury and sodium iodid had been administered without benefit. Cultures and smears made by me showed staphylococci and streptococci only. The lesions began as raised erythematous plaques from one-half to 1 inch (1.27 to 2.54 cm.) in diameter, which softened and eventually ulcerated, and healed only after a long time. The present lesions were confined mostly to the right tibial region, and the scars of the healed lesions were plainly visible. The boy's general health apparently had not suffered, as he had gained in weight and height during the past nineteen months. Various local treatment had been used. It was the opinion of the presenter that the lesions were those of a staphylococcus infection on a nonresistant skin.

ERYTHEMA FIGURATUM PERSTANS. Presented by Dr. C. D. Freeman.

A man, aged 34, whose physical examination and blood Wassermann test were negative, had always been in good health until about six years ago when he noticed a small dark red lesion about the size of a pea on the left cheek. Other lesions soon appeared and the process gradually spread in the periphery until the upper part of the cheek was practically entirely involved. Two years later a similar eruption appeared on the right cheek. The first lesions appeared on the body two years ago, one over the right scapula, of circinate character. Some of these lesions had disappeared, leaving slight pigmentation, and have again appeared and remained until the present time. There were no subjective symptoms. The lesions on the face had a decided violaceous hue.

ACTINOMYCOSIS. Presented by Dr. H. N. Klein.

A man, aged 35, a farmer, about seven months ago had a sore throat, followed two weeks later by definite swelling of the right cheek and neck which interfered with his breathing. In order to obtain relief he was sent to a surgeon to have the lump incised; after this was done the patient noticed that there was only a slight improvement and that numerous discharging sinuses remained in the region of the neck. Scrapings from the sinuses and growths on glucose agar showed the ray fungus. Under large doses of iodids and roentgen-ray treatment he showed some improvement. He had been working around infected cattle.

DISCUSSION

Dr. J. H. Stokes commented on the experience of the Section on Dermatology in the treatment of visceral actinomycosis with sodium iodid intravenously. He felt that the intravenous route had no distinctive advantages in such cases, and if there was any reaction, it was unfavorable. He preferred the administration of large doses of potassium iodid by mouth.

In referring to the use of arsphenamin, as suggested by Dr. Ormsby, Dr. Stokes said that three cases under his observation in a series of perhaps ten or twelve had shown strikingly favorable results with arsphenamin, and in one of these cases a permanently satisfactory result was secured without the use of radiotherapeutic measures. In other cases it seemed as if neo-arsphenamin had had either no effect or had hastened the decline of the patient. This was the unpredictable element in the nonspecific use of arsphenamin, to which he had called attention on other occasions.

PALMAR SYPHILID. Presented by Dr. S. W. Sweitzer.

A man, aged 45, married, acquired syphilis in 1906 and took internal treatment for several months. He had had no symptoms since, until April, 1922, when he showed an extensive palmar syphilid. The patient has received six neo-arsphenamin injections and is now being treated with mercury rubs. The lesions have remained unchanged. The Wassermann test is positive.

DISCUSSION

Dr. J. H. Stokes: I note the atrophy over the thenar eminence and the gyrate configurations, which are certainly to some extent suggestive of syphilis. On the other hand, palmar syphilids, in my experience, have not been as resistant to treatment for the disease as some syphilographers regard them. If a palmar syphilid does not show the beginnings of a definite response

after two or three arsphenamin injections, I am inclined to subject the diagnosis to critical revision. In this particular case, the patient had sustained an investigation for syphilis at our hands, with repeated negative Wassermann reactions and a negative spinal fluid. This does not eliminate the disease, and I can very well understand how he might subsequently have had a single positive Wassermann reaction. I can only say that the morphology of the lesion appeals to me as a resistant palmar eczema possibly of occupational origin rather than a syphilid.

D. D. TURNACLIFF, Secretary.

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